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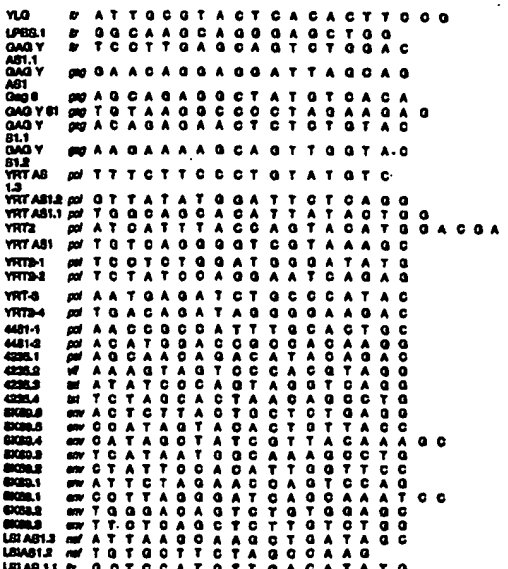
(54) Titre: SOUCHES DE VIH–1 NON–M NON–O, FRAGMENTS ET APPLICATIONS

(57) Abstract

The invention concerns retroviral strains of the group HIV–1, non–M non–O, particularly a strain called YBF30, its fragments and its applications as diagnosis reagent and as immunogenic agent. The HIV–2 different both from the group M and from the group O have the following characteristics: little or no serological response with respect to proteins of groups M and O and strong serological response with respect to proteins derived from the YBF30 strain or the SIV CPZGAB strain; absence of genomic amplification by the primers of regions *env* and *gag* of the HIV–1–1 of groups M and O; genomic amplification in the presence of the primers derived from the YBF30 strain; and homology of the envelope gene products higher than 70 % with respect to the YBF30 strain.

(57) Abrégé

Souches de rétrovirus du groupe VIH–1, non–M non–O, notamment une souche dénommée YBF30, ses fragments ainsi que ses applications, en tant que réactif de diagnostic et en tant qu'agent immunogène. Les VIH–1 distincts à la fois du groupe M et du groupe O présentent les caractéristiques suivantes: peu ou pas de réactivité sérologique vis–à–vis des protéines des groupes M et O et forte réactivité sérologique vis–à–vis des protéines issues de la souche YBF30 selon l'invention ou de la souche SIV CPZGAB; absence d'amplification génomique à l'aide des amorces des régions *env* et *gag* des VIH–1 des groupes M et O; amplification génomique en présence des amorces issues de la souche YBF30, selon l'invention; et homologie des produits du gène d'enveloppe supérieure à 70 % vis–à–vis de la souche YBF30.



ABSTRACT

Retroviral strains of the non-M, non-O HIV-1 group, in particular a strain designated YBF30, its fragments and also its uses as a diagnostic reagent and as an immunogenic agent.

The HIV-1 viruses which differ both from the M group and the O group exhibit the following characteristics:

- little or no serological reactivity with regard to the proteins of the M and O groups and strong serological reactivity with regard to the proteins which are derived from the strain YBF30 according to the invention or the strain CPZGAB SIV;
- absence of genomic amplification when using primers from the *env* and *gag* regions of the M and O HIV-1 groups;
- genomic amplification in the presence of primers which are derived from the YBF30 strain according to the invention; and
- homology of the products of the envelope gene which is greater than 70% with regard to the YBF30 strain.

NON-M, NON-O HIV-1 STRAINS, FRAGMENTS AND USES.

The present invention relates to retroviral strains of the non-M, non-O HIV-1 group, in particular a strain designated YBF30, to its fragments and to its uses as a diagnostic reagent and as an immunogenic agent.

The human acquired immunodeficiency viruses HIV-1 and HIV-2 are retrolentiviruses, which are viruses found in a large number of African primates. All these viruses appear to have a common ancestor; however, it is very difficult to prejudge the period at which these different viruses became separated from this precursor. Other viruses which are more distant, but which nevertheless belong to the same group, are found in other mammals (ungulates and felines).

All these viruses are associated with long infections; an absence of symptoms is the rule in monkeys which are infected naturally.

While the origin of HIV-2 appears to be clear on account of its strong homology with the Sooty Mangabey (West Africa) virus, no virus which is closely related to HIV-1 has been found in monkeys. The most closely related viruses are viruses found in two chimpanzees (CPZGAB SIV, ANT SIV).

All the lentiviruses have been found to exhibit substantial genetic variability, and the phylogenetic study of these variants, obtained from a large number of different geographic locations, has enabled 8 subtypes (clades) of HIV-1 to be distinguished, all of which are equidistant from each other. The clades are only a mathematical representation of the expression of the variability: phenetic analysis, which is based on the amino acids rather than on the nucleic acids, gives different results (Korber et al., 1994).

The demonstration of subtypes is in accord with a phylogenetic analysis which does not, to date, have any pathophysiological correlation but, instead, a geographical correspondance. This is because each

subtype is mainly found in a particular geographical area. The B subtype is predominant in Europe and the United States whereas two subtypes, i.e. E and B, are found in Thailand and there is a strong correlation between the mode of transmission which, in actual fact, corresponds to a particular population and the subtype found. All the clades have been found in Africa and their distribution across the rest of the world reflects a probability of encounter between persons indulging in high-risk behaviour. The main clade, which is the main one because it is present in substantial proportions in Africa, is clade A. A very great degree of variability has been found in some African countries (G. Myers, 1994; P.M. Sharp et al., 1994). Several subtypes have been characterized in the western central African countries such as the Central African Republic (Murphy et al., 1993) and Cameroon (Nkengasong et al., 1994).

Finally, patients have been characterized who are carriers of viral variants of HIV-1, whose sera have posed detection problems for particular kits which are sold on the French market and whose confirmatory Western blots have been atypical (Loussert-Ajaka et al., 1994; Simon et al., 1994; PCT International Application WO 96/27013).

Analysis of these variants has confirmed the fact that the type 1 HIV viruses should be subdivided into two groups, i.e. the M (major) group and an O (outlier) group, which includes these isolates, as Charneau et al., 1994 had proposed. Analysis of the synonymous mutations/non-synonymous mutations ratio carried out on the sequences of the known O group viruses indicates that this new group is also ancient, even if no more ancient than the M group (Loussert-Ajaka et al., 1995). Its low prevalence to date, i.e. 8% of patients infected with HIV-1 in Cameroon (Zekeng et al., 1994) and 18 cases characterized in France, is thought to be due to factors which are purely epidemiological.

These two groups of HIV-1 form a tree which is in the shape of a double star (Figures 9 to 19). Two isolates, i.e. CPZGAB SIV, characterized from a chimpanzee from Gabon (Huet et al., 1990) and CPZANT SIV, characterized from a chimpanzee in the Antwerp Zoo, possess sequences and genetic organizations which are very closely related to HIV-1 but which do not fall within either of these two groups and form two new branches on the phylogenetic tree.

The demonstration of new variants is important for developing sufficiently sensitive and specific reagents for detecting HIV infections, that is to say reagents which do not lead to false-negative or false-positive results, and for developing compositions which are protective in regard to subtypes which do not belong either to the M group or to the O group.

Consequently, the invention provides a non-M, non-O strain, as well as sequences derived from this strain, which are suitable for detecting non-M and non-O HIV-1 variants and which do not lead to false-negative or false-positive results being obtained. In order to do this, the inventors have, in particular, established an algorithm for differentiating between, and confirming, group M and group O HIV-1 infections, thereby enabling them to select non-M, non-O variants.

The present invention relates to a non-M, non-O HIV-1 strain which exhibits the morphological and immunological characteristics of the retrovirus which was deposited on 2 July 1996 under number I-1753 (designated YBF30) in the Collection Nationale de Cultures de Microorganismes (National Collection of Microorganism Cultures), kept by the Pasteur Institute.

A non-M, non-O variant is understood as meaning a type 1 HIV which cannot serologically and molecularly be recognized as belonging to either of these groups.

The present invention also relates to the complete nucleotide sequence of the strain as defined above (SEQ ID No. 1) as well as to nucleic acid

fragments which are at least 10 nucleotides in size and which are derived from the said strain.

Fragments of this type which may be mentioned are:

- YBF 30 LTR (SEQ ID No. 2),
- YBF 30 GAG (SEQ ID No. 3) (*gag* gene),
- YBF 30 POL (SEQ ID No. 5) (*pol* gene),
- YBF 30 VIF (SEQ ID No. 7) (*vif* gene),
- YBF 30 VPR (SEQ ID No. 9) (*vpr* gene),
- YBF 30 VPU (SEQ ID No. 11) (*vpu* gene),
- YBF 30 TAT (SEQ ID No. 13) (*tat* gene),
- YBF 30 REV (SEQ ID No. 15) (*rev* gene),
- YBF 30 ENV gp160 (SEQ ID No. 17) (*env* gene),
- YBF 30 NEF (SEQ ID No. 19) (*nef* gene),
- the SEQ ID Nos. 21-57, also designated, respectively, YLG, LPBS.1, GAG Y AS1.1, GAG Y AS1, GAG 6, GAG Y S1, GAG Y S1.1, GAG Y S1.2, YRT AS1.3, YRT AS1.2, YRT AS1.1, YRT 2, YRT AS1, YRT 2.1, YRT 2.2, YRT 2.3, YRT 2.4, 4481-1, 4481-2, 4235.1, 4235.2, 4235.3, 4235.4, SK69.6, SK69.5, SK69.4, SK69.3, SK69.2, SK69.1, SK68.1, SK68.2, SK68.3, LSI AS1.3, LSI AS1.2, LSI AS1.1, LSI A1, YLPA.

Such sequences can be used in the specific identification of a non-M, non-O HIV-1, and as diagnostic reagents, either alone or pooled with other reagents, for the differential identification of any HIV-1.

These sequences may, in particular, be employed in diagnostic tests which comprise either a direct hybridization with the viral sequence to be detected or an amplification of the said viral sequence, with these tests using, as primers or as probes, an oligonucleotide which comprises at least 10 nucleotides and which is included in any one of the above

sequences, in particular one of the abovementioned sequences, SEQ ID Nos. 21-57.

The present invention also relates to HIV-1 viruses which are characterized in that they differ both from the M group and from the O group and exhibit the following characteristics:

* little or no serological reactivity with regard to proteins of the M and O groups and strong serological reactivity with regard to proteins which are derived from the YBF30 strain or the CPZGAB SIV strain;

* absence of genomic amplification when using primers from the *env* and *gag* regions of HIV-1 viruses of the M and O groups;

* genomic amplification in the presence of primers which are derived from the YBF30 strain, as defined above; and

* homology of the products of the envelope gene which is > 70% with regard to the YBF30 strain.

The invention also relates to the use of the above described sequences for implementing a method of hybridization and/or of gene amplification of nucleic acid sequences of the HIV-1 type, with these methods being applicable to the in-vitro diagnosis of the potential infection of an individual with a virus of the non-M, non-O HIV-1 type.

This in-vitro diagnostic method is carried out using a biological sample (serum or circulating lymphocyte) and comprises:

. a step of extracting the nucleic acid which is to be detected and which belongs to the genome of the virus, which virus may possibly be present in the biological sample, and, where appropriate, a step of treating the nucleic acid using a reverse transcriptase, if this nucleic acid is in RNA form,

. at least one cycle comprising the steps of denaturing the nucleic acid, of hybridizing with at least one sequence in accordance with the invention and, where appropriate, extending the hybrid, which has

been formed, in the presence of suitable reagents (polymerizing agent, such as DNA polymerase and dNTP), and

. a step of detecting the possible presence of the nucleic acid belonging to the genome of a virus of the non-M, non-O HIV-1 group type.

The following conditions are employed for the PCR using the primers derived from the YBF30 strain:

- extracting the lymphocytic DNA by means of the phenol/chloroform technique and quantifying it by spectrophotometry at a wavelength of 260 nm. All the amplifications are carried out using a Perkin Elmer 2400 thermocycler.

- the long (9 kb) PCRs are carried out using an XL PCR kit (Perkin Elmer) in accordance with the manufacturer's conditions and using the dNTP's, the buffers provided and Perkin Elmer's "hot start"; the amplification cycles of this long PCR are:

. 1 cycle of denaturation for 2 minutes at 94°C,

. then 16 cycles: 15 seconds at 94°C, 15 seconds at 55°C, 8 minutes at 68°C,

. then 24 cycles: 15 seconds at 94°C, 15 seconds at 55°C, 8 minutes at 68°C, adding a further 15 seconds (incrementation) to each cycle.

- the nested PCRs are carried out on the amplification products of the long PCRs. The conditions for carrying out the nested PCRs are as follows:

. "Expand High Fidelity PCR System" Taq polymerase buffer and enzyme from Boehringer Mannheim in accordance with the manufacturer's instructions, dNTP and "hot start" from Perkin Elmer,

. 200 µmol of each dNTP, 20 pmol of each primer in accordance with the invention, 5 µl of DNA, 10 µl of 10 × PCR buffer and 2.6 units of Taq polymerase in a volume of 100 µl,

. amplification: one cycle of 2 minutes at 94°C followed by 38 cycles: 15 seconds at 94°C, 15 seconds at 55°C, a time of elongation at 72°C which varies in

accordance with the size of the PCR product to be amplified (from 30 seconds to 2 minutes) and a final elongation cycle of 10 minutes at 72°C.

The amplified product is preferably detected by direct sequencing.

The invention also relates to a peptide or a peptide fragment which is characterized in that it can be expressed by a non-M, non-O HIV-1 strain or using a nucleotide sequence as defined above, and in that it is capable: (1) of being recognized by antibodies which are induced by a non-M, non-O HIV-1 virus, as defined above, in particular the YBF30 strain or a variant of this strain, and which are present in a biological sample which is obtained following an infection with a non-M, non-O HIV-1 strain, and/or (2) of inducing the production of anti-non-M, non-O HIV-1 antibodies.

Peptides of this type which may be mentioned are, in particular, those which are derived from the YBF30 strain, in particular: that which is expressed by the *gag* gene (SEQ ID No. 4), that which is expressed by the *pol* gene (SEQ ID No. 6), that which is expressed by the *vif* gene (SEQ ID No. 8), that which is expressed by the *vpr* gene (SEQ ID No. 10), that which is expressed by the *vpu* gene (SEQ ID No. 12), that which is expressed by the *tat* gene (SEQ ID No. 14), that which is expressed by the *rev* gene (SEQ ID No. 16), that which is expressed by the *env* gene (SEQ ID No. 18), or one of its fragments such as a fragment of the V3 loop region, i.e. CTRPGNNTGGQVQIGPAMTFYNIEKIVGDIRQAYC (SEQ ID No. 58), and that which is expressed by the *nef* gene (SEQ ID No. 20), or a fragment of these peptides which are capable of recognizing the antibodies which are produced during an infection with a non-M, non-O HIV-1 as defined above.

The invention also relates to immunogenic compositions which comprise one or more translation products of the nucleotide sequences according to the invention and/or one of the peptides as defined above, obtained, in particular, by synthetic means.

The invention also relates to the antibodies which are directed against one or more of the above-described peptides and to their use for implementing methods for the in-vitro, in particular differential, diagnosis of the infection of an individual with a virus of the HIV-1 type using methods which are known to the skilled person.

The present invention encompasses all the peptides which are capable of being recognized by antibodies which are isolated from an infectious serum which is obtained after an infection with a non-M, non-O HIV-1 strain, and the peptides which are capable of being recognized by an antibody according to the invention.

The invention furthermore relates to a method for the in-vitro diagnosis of a non-M, non-O HIV-1 virus, which method is characterized in that it comprises bringing a biological sample, which has been taken from a patient, into contact with antibodies according to Claim 10, which may possibly be combined with anti-CPZGAB SIV antibodies, and detecting the immunological complexes which are formed between the HIV-1 antigens, which may possibly be present in the biological sample, and the said antibodies.

The invention also relates to a kit for diagnosing HIV-1, which kit is characterized in that it includes at least one reagent according to the invention.

Apart from the provisions which have been described above, the invention also comprises other provisions which will be evident from the description which follows and which refers to examples of implementing the method which is the subject of the present invention and also to the attached drawings, in which:

- Figures 1 to 7 illustrate the location of the different primers on the genome of the YBF30 strain;

- Figure 8 illustrates the genomic organization of the YBF30 strain;

- Figures 9 to 16 depict the phylogenetic analysis of the different genes of the YBF30 strain as compared with group M HIV-1 and group O HIV-1 (Figure 9: *ltr* gene, Figure 10: *gag* gene, Figure 11: *tat* gene, Figure 12: *rev* gene, Figure 13: *vif* gene, Figure 14: *env* gp120 gene, Figure 15 *env* gp41 gene, Figure 16: *nef* gene, Figure 17: *pol* gene, Figure 18: *vpr* gene, Figure 19: *vpu* gene);
- Figure 20 illustrates the percentage genetic distance between YBF30 and HIV-1/CPZGAB SIV.

It should of course be understood, however, that these examples are give solely by way of illustrating the subject-matter of the invention, of which they in no way constitute a limitation.

For the purposes of this specification it will be clearly understood that the word "comprising" means "including but not limited to", and that the word "comprises" has a corresponding meaning.

All references, including any patents or patent applications, cited in this specification are hereby incorporated by reference. No admission is made that any reference constitutes prior art. The discussion of the references states what their authors assert, and the applicants reserve the right to challenge the accuracy and pertinency of the cited documents. It will be clearly understood that, although a number of prior art publications are referred to herein, this reference does not constitute an admission that any of these documents forms part of the common general knowledge in the art, in Australia or in any other country.

EXAMPLE : Obtaining a non-M, non-O HIV-1 variant according to the invention (YBF30) and its uses.

This was, in particular, possible in connection with studying the epidemiology of infection with human acquired immunodeficiency viruses (HIV) in Cameroon, which epidemiology is especially paradoxical. In this country,

the diversity of the strains is remarkable as most of the subtypes of the M (major) group of HIV-1 viruses known to date have been reported. Cases of infection with highly divergent HIV-1 viruses of the O group (O for outlier) have been reported, almost exclusively in patients of Cameroonian origin. Cases of infection with HIV-2, HTLV-1 and HTLV-2 subtypes A and B have also been reported.

Taking a basis the results of previous serological and genotypic assessments, the inventors established an algorithm for differentiating between and confirming infections with HIV-1 viruses of the M and O groups in order to select non-M, non-O variants.

These methods were applied to samples which were went to the National Reference Laboratory for HIV infections at Yaoundé and made it possible to characterize a highly divergent HIV isolate and to define the tools for characterizing a new HIV-1 group,

taking into account the homologies which were observed between this human strain YBF30 and the simian strain CPZGAB SIV.

I- Way of serologically characterizing the YBF30 variant during the epidemiological study.

1) Collecting the samples:

All the adult patient sera which were sent to the Yaoundé reference laboratory in 1994 and 1995 for detecting or confirming an HIV infection were studied (n = 8831).

2) Differentiating serologically between group M and group O HIV-1, and selecting variants:

If there was positive detection of anti-HIV antibodies (Génélavia Mixt indirect mixed HIV-1 and HIV-2 EIA, Sanofi-Pasteur, Paris, France), this was then combined with an EIA test based on the principle of competition with a specific antigen of the M group (Wellcozyme Rec HIV-1, Murex, Dartford, UK).

If the competitive Wellcozyme Rec HIV-1 test is positive, with a ratio for the reactivity in optical density (OD) as compared with the threshold or *cut-off* (CO) value which is greater than 5 (CO/OD > 5), the serum is regarded as being HIV-1-positive, a result which should be confirmed on a new sample.

The choice of a reactivity ratio which is greater than 5 for regarding the competitive test as being a test for confirming infection with HIV-1 is based on experience acquired by the virology laboratory of Bichat hospital: all of 7200 samples which reacted with a ratio > 5 gave a strongly positive HIV-1 Western blot (WB, New Lav Blot 1, SDP, Marnes la Coquette). Apart from cases of HIV-1 seroconversion, the samples which are confirmed as being HIV-positive and which give a Wellcozyme ratio of < 5 correspond either to infections with HIV-2 or to infections with O group HIV-1 or other HIV-1 variants.

In order to eliminate the false-positive reactions when carrying out a mixed EIA detection, the samples which give a CO/OD ratio of < 5 are tested

systematically with a third generation mixed HIV-1/HIV-2 EIA (Enzygnost Plus, Marburg, Germany) which includes antigens of the M and O HIV-1 groups (recombinant gp41 of the MVP5180 strain). If this test is positive, a rapid test which discriminates between HIV-1 and HIV-2 (Multispot, SDP, Marnes la Coquette) and a Western blot (WB, New Lav Blot 1 or 2, SDP) are then carried out.

3) Serologically confirming infections with O group HIV-1 and HIV-1 variants.

All the samples which give a CO/OD ratio of < 5, and which have been differentiated as being positive by WB (positivity criteria: 2 ENV +/- POL +/- GAG or 1 ENV + POL +/- GAG) and HIV-1, are tested with a dot blot test using peptide antigens of the V3 and transmembrane regions (InnoLia, Innogenetics, Ghent, Belgium).

4) Retroviral isolation of the group O and variant strains.

The peripheral blood mononuclear cells (PBMC) from the seropositive patients were isolated by Ficoll-Hypaque gradient in Cameroon and then stored, and transported to Paris, in liquid nitrogen.

After thawing, the PBMCs from the patients were cocultured together with lymphocytes from seronegative Caucasian donors. Viral replication in the culture supernatants was demonstrated by detecting reverse transcriptase activity and by carrying out tests for detecting the p24 antigen (Elavia p24 polyclonal, SDP) over a period of one month.

5) Sequences:

The PCR products are visualized on agarose gels of from 1 to 1.4% concentration, depending on the size of the fragments, precipitated in 3M sodium acetate (1:10) and 3 volumes of absolute ethanol, incubated at -80°C for 30 minutes and then centrifuged at 13,000 rpm for 20 minutes. The pellet is dried and then taken up in 10 µl of distilled water (Sigma). Purification is carried out on a "Qiaquick Gel Extraction kit" (Qiagen) in accordance with the manufacturer's instructions; the

products are sequenced on an automated DNA sequencer (Applied Biosystems, Inc., Foster City, CA) using an Applied Biosystem Dye Terminator kit, as previously described (Loussert-Ajaka et al., 1995); the nucleotide sequences are analysed on Sequence Navigator software (Applied Biosystems), and aligned using GeneWorks software (Intelligenetics Inc.).

6) Phylogenetic analyses:

The sequences were aligned using the CLUSTAL software for multiple alignments and taking, as the reference matrix, the alignments of the compilation of HIV sequences possessed by the Laboratory of Biology and Theoretical Biophysics, Los Alamos, New Mexico, 87545 USA.

The phylogenetic analyses were performed using the PHYLIP software; the distances were firstly calculated using DNADIST, after which the phylogenetic analysis was carried out using NEIGBOR JOINING or FITCH; finally, the trees were drawn using DRAWTREE (Figures 9 to 19). The genetic distance percentages are also shown in Figure 20.

SEQBOOT was first of all used for the "*bootstrapping*" analyses, followed by DNADIST and NEIGHBOR JOINING or FITCH. Finally, the *bootstrap* values were obtained using CONSENS.

II - Results of the investigation for detecting group O and variant HIV viruses:

174 samples, out of 3193 samples found to be positive in the screening, were regarded as being group O or group M with abnormal serological reactivity or as being variants.

III - Detection of a non-group O and non-group M sample exhibiting abnormal serological reactivity

The 174 sera which were HIV-1-positive by WB (Western blot), but reactive with a CO/OD ratio of < 5 in the competitive EIA, were tested by differential LIA dot blot on the V3 peptides from group M, group O and CPZGAB SIV:

- 7 do not react with any of the peptides represented (M, O or CPZGAB SIV). The absence of any cell collection does not allow any conclusion to be drawn.

- 82 give a reactivity with regard to at least one of the peptides corresponding to the V3 loop of O group strains. The frequency of the crossreactions is low and restricted to the epitopes which correspond to the consensus V3 regions (11%) and to the CPZGAB SIV V3 regions (43%).

- 84 sera do not react with the O group epitopes. Most of these samples were obtained from patients exhibiting an AIDS syndrome (75/84).

- one serum, which was taken from a Cameroonian patient (NJ) reacts exclusively with the CPZGAB SIV peptide. This isolated reactivity with regard to a CPZGAB SIV antigen has never been described previously. Since lymphocytes had been collected from the patient, it was possible to continue with the virological characterization of this strain, which was termed YBF30.

IV - Results of the serological and virological examinations performed on the first samples taken from this patient (May 1995) (serum No.: 95-6295):

1) Commercial ELISA tests (optical density/threshold value)

Criterion of positivity: OD/CO > 1

Génélavia = > 15

Wellcozyme CO/OD = 1.55

Abbott Plus = > 15

Behring Plus = 4.2

2) Western blot

New Lav 1 Pasteur WB:

160++, 120++, 68++, 55+, 41+, 40+/-, 34++, 24++, 18+

3) Innogenetics LIA dot blot

Negative for all the group O and group M bands apart from CPZGAB SIV V3

4) Results of the investigative serological examinations carried out on peptides which are specific for the M and O groups

The technique developed by Professor Francis Barin of the Virology Laboratory of the Tours CHU was modified (Barin F. et al., 1996); use was made of synthesized transmembrane region peptides (BioMérieux) for developing a test for differentiating between the M and O groups. This technique is based on antibody-binding competition between the transmembrane gp41 peptides of the O and M groups, which are deposited on the solid phase, and gp41 transmembrane peptides either of the O group or of the M group at higher concentration in a hyperosmolar liquid reaction phase. The results are shown in Table I below, in which the CP well corresponds to the 100% inhibition control and the CSP well corresponds to the 0% inhibition control.

Table I

Results of the inter-group O-group M differentiations for the 6295 serum

	gp41 M	gp41 O	CP	CSP
6295	0.25	0.36	0.12	1.98

These results demonstrate that there is strong binding with regard to the peptides of the solid phase (CSP) and a marked inhibition due to the combined addition of the M and O peptides (CP), but no clear differentiation either by the M peptide or by the O peptide. This is, therefore, serological evidence that the infecting strain does not belong either to the M group or to the O group.

In view of an isolated reactivity in the InnoLia dot blot with regard to the CPZGAB SIV V3 antigens, on the same bases of competition between peptides, this serum was studied by bringing into competition the gp41 M, gp41 O and gp41 CPZGAB SIV peptides.

Use of the serum from the chimpanzee named 'Amandine' (donated by M. Peeters, who isolated the

CPZGAB SIV strain, AIDS 1992) initially enabled this technique to be validated. In Table II, the lowest values (OD) indicate the highest degree of binding to the antigens.

Table II

Results of the inter-group O-group M-CPZGAB SIV differentiations using the Amandine chimpanzee serum and the 6295 serum

	gp41 M	gp41 O	gp41 CPZGAB	CP	CSP
Amandine	0.8	1.4	0.3	0.5	1.9
6295	0.7	1.1	0.7	0.4	2.1

The reactivity of the "Amandine" serum confirms and validates the test according to the invention and shows that, while the serum of the patient reacts identically with regard to the M and CPZGAB SIV peptides, it does not exhibit a crossreaction with the O peptide.

These results demonstrate that the group M gp41 and CPZGAB SIV gp41 peptides exert a similar inhibition on the serum of the patient. The antigens of the infecting strain have therefore given rise to antibodies which recognize the group M and CPZGAB SIV gp41 peptides in a similar manner.

4) Results obtained from the lymphocyte isolation (sampling of May 1995)

A retrovirus was isolated, using standard techniques, from the lymphocytes which were sampled on 22 May 1995. Culture using the MT2 cell line shows that the YBF30 strain does not form any syncytia (NSI).

V - Results of the serological examinations carried out on the second blood sample (November 1995) (serum No. 95-3371)

1) Innogenetics LIA dot blot

Negative for all the bands, apart from CPZGAB SIV V3

2) Results of the investigative serological examinations carried out on the peptides specific for the M and O groups.

Table III shows the results of the inter-group O-group M-CPZGAB SIV gp41 differentiations using the 3371 serum.

Table III

Results of the inter-group O-group M-CPZGAB SIV gp41 differentiations using the 3371 serum

	gp41 M	gp41 O	gp41 CPZGAB	CP	CSP
3371	1.31	1.7	0.89	0.54	2.02

These results confirm, on this new blood sample (taken from the same patient in the terminal stage of the disease), that the CPZGAB SIV gp41 peptide markedly inhibits the serum of the patient.

The antigens of the infecting strain have therefore induced antibodies which preferentially recognize the CPZGAB SIV gp41 peptide.

3) Results from the lymphocyte isolation (blood sampling of November 95 (95-3371-YBF31))

A retrovirus was isolated, using the standard techniques, from the lymphocytes which were sampled in November 1995 and termed YBF31; the sequence elements are identical to those of YBF30.

VI - Genomic amplification and sequences of YBF30

The DNA for all the PCR manipulations is extracted from the cells obtained at the end of a positive culture.

The PCRs carried out using the O group HIV-1 primers are negative in the different regions tested (*gag, pol, env*). Similarly, those carried out using the primers which are specific for M group HIV-1 are also negative.

The amplification and hybridization conditions for the O group PCRs are those described in Loussert-Ajaka, 1995. The amplification and hybridization conditions for the M group PCRs are those described by the authors cited below.

These M group primers are located in accordance with the HIV-1 HXB2 sequence as follows:

- in *env* gp120: ED3/ED12 (position 5956-5985; 7822-7792); ED5/ED14 (6556-6581; 7960-7931); ED5/ED12; ED3/ED14; ES7/ES8 (7001-7020; 7667-7647) (Delwart et al. Science 1993; 262: 1257-1261).

- in *env* gp41: first PCR, ED3/M29, followed by a nested PCR, M28/M29 (7785-7808; 8099-8124); M28/M29 have the following sequences:

M28: CGGTTCTT(AG)GGAGCAGC(ACT)GGAAGCA,

M29: T(CT)T(ACGT)TCCCA(CT)T(AT)(CT)A(AGT)CCA(AGT)GTCAT;

SK68/SK69 (Ou et al. Science, 1988; 239: 295-297).

- in *gag*: Amplicor Roche Diagnostics systems; nested *gag* primers (Loussert-Ajaka et al. Lancet 1995; 346: 912-913); SK38/SK39 (Ou et al., Science, 1988; 239: 295-297).

- in *pol*: A/NE1 (Boucher et al., Lancet, 1990; 336: 585-590); Pol3/Pol4 (Lauré et al., Lancet, 1988, ii, 538-541).

Only the PCRs carried out using the H Pol primers (4235/4538) are positive, with this being followed by a nested PCR using the primers 4327/4481 (Fransen et al., Molecular and Cellular Probes 1994; 8: 317-322). This H Pol fragment, which is located in the integrase (260 bp), has been sequenced. Amplification using the HPOL primers is made possible due to the excess of virus. This is because the DNA which is used is extracted from cells at the end of a strongly positive culture (reverse transcriptase > 100,000 cpm). It is not possible to amplify the DNA which is extracted from fresh cells without coculture because of the large number of mispairings between the HPOL primers (especially in the 3' region) and the sequence of the YBF30 isolate. Conservation of this 3' end is very important for the extension activity of the Taq polymerase.

1 - Sequence of the *pol* gene: the use of very degenerate primers for amplifying, by RT-PCR, the RNA

extracted from the positive culture supernatant gave a positive amplification. These are primers which are common to all retroviruses (Donehower et al. J. Virol. Methods 1990; 28: 33-46), and are located in the reverse transcriptase region of the *pol* gene. Analysis of the fragment after sequencing made it possible to generate a specific primer, i.e. YRT2 (SEQ ID No.32), from the YBF30 isolate and to amplify the *pol* gene using the Hpol 4481 primer (Fransen et al., 1994, loc. cit.) as the antisense primer. The fragment was sequenced by synthesizing specific primers as required for each fragment generated (Figure 1).

2 - Sequence of the *env* gene: the second approach was to perform a long PCR (XL-PCR, Perkin Elmer), thereby amplifying all the virus (9000 bp) using primers situated in the LTR: LPBS 1 (SEQ ID No.22); LSiGi, followed by a 6000 bp nested PCR using YRT2 (SEQ ID No.32)/SK69, and to sequence all the envelope following the same procedure. The gp41 region was sequenced using a nested PCR and employing the primers SK68/LSiGi.

3 - Sequence of the *gag* gene: use of a nested PCR, achieved by means of a long PCR (LPBS 1/LSiGi), employing the primers Gag 5 and Gag 11i, and generating from this specific primers, as required, in order to walk along the viral genome.

VII - Results of the sequencings

The strain YBF30 was sequenced completely (see list of sequences). The YBF31 strain of November 1995 was sequenced in part, and the absence of significant variation confirms the validity of the YBF30 sequences.

VIII - Synthesizing peptides of the V3 loop region of the YBF30 strain.

Studying the sequences of the V3 loop region made it possible to synthesize the corresponding peptide and to compare the amino acids of this region of the YBF30 strain with those of other M subtypes and O strains.

The sequences of the peptides are:

YBF30: SEQ ID No.58

CPZGAB SIV: CHRPGNNTRGEVQIGPGMTFYNIENVYGDTRSAYC (SEQ ID No.59)

GROUP O: (ANT70) CIRPGNRTYRNLQIGPGMTFYNVEIATGDIRKAFC (SEQ ID No.60)

GROUP M: (SS-TYPE A) CTRPNNNTRKSVRIGPGQAFYATGDIIGDIRQAHC (SEQ ID No.61)

The peptide was synthesized, starting with the two asparagines of the 5' region of the loop, and used in accordance with the same principle as previously described (see IV 4)), namely in competition in relation to the peptides of the M group, the O group and CPZGAB SIV. The results shown in Table IV confirm the original nature of this strain and the possible spread of these strains, since the serological results favour infection of the YBF30 type in Cameroon. Furthermore, a study of 200 selected HIV-1-positive sera from Cameroon provides evidence of a new case exhibiting a profile which is similar to that of YBF30.

Table IV

Study of the reactivity of 200 sera

Serum	Origin	V3A	V3cpz	V3YBF30	CP	CSP
953371	Cameroon	1.66	0.38	1.39	0.39	1.64
956295	Cameroon	1.72	0.37	1.16	0.51	1.73
967321	Cameroon	0.07	0.17	0.5	0.05	0.27
Amandine	GABSIV	1.74	0.14	1.48	0.19	1.74
NOA.*	ANTSIV	2.66	0.31	1.88	0.46	1.9

* serum from CPZ ANT SIV

The reactivity of the sera 953371 and 956295, corresponding to the patient from whom the YBF30 strain was isolated, with the CPZ SIV peptide, was confirmed in this new test. The lower reactivity with regard to its own V3 antigen is usual during the late stages of the disease. Nevertheless, this reactivity remains greater than that raised with regard to the M peptide. Another Cameroonian patient (serum 967321) exhibits the same profile of peptide reactivity.

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As is evident from the above, the invention is in no way limited to those of its embodiments which have just been described more explicitly; on the contrary, it encompasses all the variants which may come to the mind of the skilled person without departing from the context or scope of the present invention.

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(ii) TITLE OF INVENTION: NON-M NON-O, HIV STRAINS, FRAGMENTS AND USE.

(iii) NUMBER OF SEQUENCES: 61

(iv) COMPUTER READABLE FORM:
(A) MEDIUM TYPE: Floppy disk
(B) COMPUTER: IBM PC compatible
(C) OPERATING SYSTEM : PC-DOS/MS-DOS
(D) SOFTWARE: PatentIn Release #1.0, Version #1.30 (OEB)

(2) INFORMATION FOR SEQ ID NO: 1:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 9183 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: ADN (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 1:

CTTCTCGCTT GTACTGGGTC TCTCTTGCTG GACCAGATTA GAGCCTGGGA GCTCTCTGGC 60

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AACCACTGAG CTAACAGATA AAAAGAAGCA AGTTTACTCT CTGTTTTATG TAGAAGATGT 6360

AGTACCAATC AATGCCTATA ATAAAACATA TAGGCTAATA AATTGTAATA CCACAGCTGT 6420

GACACAAGCT TGTCCTAAGA CTTCCTTTGA GCCAATTCCA ATACATTACT GTGCACCACC 6480

AGGCTTTGCC ATTATGAAAT GTAATGAAGG AAACTTTAGT GGAAATGGAA GCTGTACAAA 6540

TGTGAGTACT GTACAATGCA CACATGGAAT AAAGCCAGTG ATATCCACTC AGTTAATCCT 6600

AAATGGAAGC TTAAATACAG ATGGAATTGT TATTAGAAAT GATAGTCACA GTAATCTGTT 6660

GGTGCAATGG AATGAGACAG TGCCAATAAA TTGTACAAGG CCAGGAAATA ATACAGGAGG 6720

ACAGGTGCAG ATAGGACCTG CTATGACATT TTATAACATA GAAAAAATAG TAGGAGACAT 6780

TAGACAAGCA TACTGTAATG TCTCTAAAGA ACTATGGGAA CCAATGTGGA ATAGAACAAG 6840

AGAGGAAATA AAGAAAATCC TGGGGAAAAA CAACATAACC TTCAGGGCTC GAGAGAGGAA 6900

TGAAGGAGAC CTAGAAGTGA CACACTTAAT GTTCAATTGT AGAGGAGAGT TTTTCTATTG 6960

TAACACTTCC AAATTATTTA ATGAGGAATT ACTTAACGAG ACAGGTGAGC CTATTACTCT 7020

GCCTTGTAGA ATAAGACAGA TTGTAAATTT GTGGACAAGG GTAGGAAAAG GAATTTATGC 7080

ACCACCAATT CGGGGAGTTC TTAACTGTAC CTCCAATATT ACTGGACTGG TTCTAGAATA 7140

TAGTGGTGGG CCTGACACCA AGGAAACAAT AGTATATCCC TCAGGAGGAA ACATGGTTAA 7200

TCTCTGGAGA CAAGAGTTGT ATAAGTACAA AGTAGTTAGC ATAGAACCCA TAGGAGTAGC 7260

ACCAGGTAAA GCTAAAAGAC GCACAGTGAG TAGAGAAAAA AGAGCAGCCT TTGGACTAGG 7320

TGCGCTGTTT CTTGGGTTTC TTGGAGCAGC AGGGAGCACT ATGGGCGCAG CGTCAATAAC 7380

GCTGACGGTA CAGGCCCGGA CATTATTATC TGGGATAGTG CAACAGCAGA ATATTCTGTT 7440

GAGAGCAATA GAGGCGCAAC AACATTTGTT GCAACTCTCA ATCTGGGGCA TTAAACAGCT 7500

CCAGGCAAAA GTCCTTGCTA TAGAAAGATA CCTTAGGGAT CAGCAAATCC TAAGTCTATG 7560

GGGCTGCTCA GGAAAAACAA TATGCTATAC CACTGTGCCT TGGAATGAGA CTTGGAGCAA 7620

CAATACCTCT TATGATACAA TCTGGAATAA TTTAACCTGG CAACAATGGG ATGAGAAAGT 7680

AAGAAACTAT TCAGGTGTCA TTTTTGGACT TATAGAACAG GCACAAGAAC AACAGAACAC 7740

AAATGAGAAA TCACTCTTGG AATTGGATCA ATGGGACAGT CTGTGGAGCT GGTTTGGTAT 7800

TACAAAATGG CTGTGGTATA TAAAAATAGC TATAATGATA GTAGCAGGCA TTGTAGGCAT 7860

AAGAATCATA AGTATAGTAA TAACTATAAT AGCAAGAGTT AGGCAGGGAT ATTCTCCCCT 7920

TTCGTTGCAG ACCCTTATCC CAACAGCAAG GGGACCAGAC AGGCCAGAAG AAACAGAAGG 7980

AGGCGTTGGA GAGCAAGACA GAGGCAGATC CGTGCGATTA GTGAGCGGAT TCTCAGCTCT 8040

TGTCTGGGAG GACCTCCGGA ACCTGTTGAT CTTCCTCTAC CACCGCTTGA CAGACTCACT 8100

CTTGATACTG AGGAGGACTC TGGAACTCCT GGGACAGAGT CTCAGCAGGG GACTGCAACT 8160

ACTGAATGAA CTCAGAACAC ACTTGTGGGG AATACTTGCA TATTGGGGAA AAGAGTTAAG 8220

GGATAGTGCT ATCAGCTTGC TTAATACAAC AGCTATTGTA GTAGCAGAAG GAACAGATAG 8280

GATTATAGAA TTAGCACAAA GAATAGGAAG GGGAATATTA CACATACCTA GAAGAATCAG 8340

ACAAGGCCTA GAAAGAGCAC TGATATAAGA TGGGAAAGAT TTGGTCAAAG AGCAGCCTAG 8400

TAGGATGGCC AGAAATCAGA GAAAGAATGA GAAGACAAAC GCAAGAACCA GCAGTAGAGC 8460

CAGCAGTAGG AGCAGGAGCA GCTTCTCAAG ATCTAGCTAA TCGAGGGGCC ATCACCATAA 8520

GAAATACTAG AGACAATAAT GAAAGTATAG CTTGGCTAGA AGCACAAGAA GAAGAAGAGG 8580

AAGTAGGCTT TCCAGTACGC CCTCAGGTAC CATTAAGGCC AATAACCTAT AAACAGGCTT 8640

TTGATCTTTC CTTCTTTTTA AAAGATAAGG GGGGACTGGA AGGGCTAGTT TGGTCCAGAA 8700

AAAGGCAAGA TATTCTAGAC CTCTGGATGT ATCACACACA AGGCATCCTC CCTGACTGGC 8760

ATAACTACAC ACCAGGGCCA GGAATTAGAT ACCCCGTAAC CTTTGGATGG TGCTTCAAAC 8820

TAGTACCATT GTCAGCTGAA GAAGTAGAAG AGGCTAATGA AGGAGACAAC AATGCCCTCT 8880

TACACCCCAT ATGTCAACAT GGAGCAGATG ATGATCATAA AGAAGTGTTG GTGTGGCGAT 8940

TTGACAGCTC CCTAGCAAGA AGACATGTAG CAAGAGAGCT GCATCCGGAG TTTTACAAGA 9000

ACTGCTGACA AGGGACTTTA CTGCTGACAA GGGACTTTAT ACTTGGGGAC TTTCCGCCAG 9060

GGACTTTCCA GGGAGGTGTG GTTGGGGGAG TGGCTTGCCC TCAGAGCTGC ATAAAAGCAG 9120

CCGCTTCTCG CTTGTACTGG GTCTCTCTTG CTGGACCAGA TTAGAGTCTG GGAGCATATT 9180

GGG 9183

(2) INFORMATION FOR SEQ ID NO: 2:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGHT: 813 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: ADN (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 2:

TTGGAAGGGC TAGTTTGGTC CAGAAAAAGG CAAGATATTC TAGACCTCTG GATGTATCAC 60

ACACAAGGCA TCCTCCCTGA CTGGCATAAC TACACACCAG GGCCAGGAAT TAGATACCCC 120

GTAACCTTTG GATGGTGCTT CAAACTAGTA CCATTGTCAG CTGAAGAAGT AGAAGAGGCT 180

AATGAAGGAG ACAACAATGC CCTCTTACAC CCCATATGTC AACATGGAGC AGATGATGAT 240

CATAAAGAAG TGTTGGTGTG GCGATTTGAC AGCTCCCTAG CAAGAAGACA TGTAGCAAGA 300

GAGCTGCATC CGGAGTTTTA CAAGAACTGC TGACAAGGGA CTTTACTGCT GACAAGGGAC 360

TTTATACTTG GGGACTTTCC GCCAGGGACT TTCCAGGGAG GTGTGGTTGG GGGAGTGGCT 420

TGCCCTCAGA GCTGCATAAA AGCAGCCGCT TCTCGCTTGT ACTGGGTCTC TCTTGCTGGA 480

CTATACAGAT TAGAGCCTGG GAGCTCTCTG GCTAGCAGGG AACCCACTGC TTAAGCCTCA 540

ATAAATACAG CTTGCCTTGA GTGCTAAAGT GGTGTGTGCC CATCCATTCG GTAACTCTGG 600

TACCTAGAGA ATCCCTCAGA CCATCTAGAC TGAGTGAAAA ATCTCTAGCA GTGGCGCCCG 660

AACAGGGACT TAGTTGAAAA CGAAAGTAGA ACCGGAGGCT GAATCTCTCG ACGCAGGACT 720

CGGCTCGTTG GTGCACACAG CGAGAGGCGA GGCGGCGGAA GTGTGAGTAC GCAATTTTGA 780

CTGGCGGTGG CCAGAAAGTA GGAGAGAGGG AGG 813

(2) INFORMATION FOR SEQ ID NO: 3:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 1539 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: ADN (genomic)

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION:1..1536

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 3:

```
ATG GGT GCG AGA GCG TCA GTG TTA ACA GGG GGA AAA TTA GAT CAA TGG      48
Met Gly Ala Arg Ala Ser Val Leu Thr Gly Gly Lys Leu Asp Gln Trp
  1               5                  10                  15

GAA TCA ATT TAT TTG AGA CCA GGG GGA AAG AAA AAA TAC AGA ATG AAA      96
Glu Ser Ile Tyr Leu Arg Pro Gly Gly Lys Lys Lys Tyr Arg Met Lys
             20                  25                  30

CAT TTA GTA TGG GCA AGC AGG GAG CTG GAA AGA TTC GCT TGT AAC CCA     144
His Leu Val Trp Ala Ser Arg Glu Leu Glu Arg Phe Ala Cys Asn Pro
         35                  40                  45

GGT CTC ATG GAC ACA GCG GAC GGC TGT GCC AAG TTA CTA AAT CAA TTA     192
Gly Leu Met Asp Thr Ala Asp Gly Cys Ala Lys Leu Leu Asn Gln Leu
     50                  55                  60

GAA CCA GCT CTC AAG ACA GGG TCA GAA GAA CTG CGC TCT TTA TAT AAC     240
Glu Pro Ala Leu Lys Thr Gly Ser Glu Glu Leu Arg Ser Leu Tyr Asn
 65                  70                  75                  80

GCT CTA GCA GTT CTT TAT TGT GTC CAT AGT AGG ATA CAG ATA CAC AAC     288
Ala Leu Ala Val Leu Tyr Cys Val His Ser Arg Ile Gln Ile His Asn
                 85                  90                  95

ACA CAG GAA GCT TTG GAC AAG ATA AAA GAG AAA CAG GAA CAG CAC AAG     336
Thr Gln Glu Ala Leu Asp Lys Ile Lys Glu Lys Gln Glu Gln His Lys
            100                 105                 110

CCC GAG CCA AAA AAC CCA GAA GCA GGG GCA GCG GCA GCA ACT GAT AGC     384
Pro Glu Pro Lys Asn Pro Glu Ala Gly Ala Ala Ala Ala Thr Asp Ser
        115                 120                 125

AAT ATC AGT AGG AAT TAT CCT CTA GTC CAG ACT GCT CAA GGA CAA ATG     432
Asn Ile Ser Arg Asn Tyr Pro Leu Val Gln Thr Ala Gln Gly Gln Met
    130                 135                 140

GTA CAT CAG CCG CTG ACA CCC AGA ACC TTA AAT GCT TGG GTG AAA GTG     480
Val His Gln Pro Leu Thr Pro Arg Thr Leu Asn Ala Trp Val Lys Val
145                 150                 155                 160

ATA GAG GAG AAG GCC TTT AGT CCA GAA GTA ATA CCA ATG TTT ATG GCC     528
Ile Glu Glu Lys Ala Phe Ser Pro Glu Val Ile Pro Met Phe Met Ala
                165                 170                 175

TTG TCA GAA GGG GCA ACG CCC TCA GAT CTA AAT ACT ATG TTA AAT ACA     576
Leu Ser Glu Gly Ala Thr Pro Ser Asp Leu Asn Thr Met Leu Asn Thr
            180                 185                 190

GTA GGG GGA CAT CAG GCA GCA ATG CAG ATG CTG AAG GAA GTC ATC AAT     624
Val Gly Gly His Gln Ala Ala Met Gln Met Leu Lys Glu Val Ile Asn
        195                 200                 205

GAG GAA GCA GCA GAC TGG GAT AGG ACA CAT CCA GTC CCT GTG GGA CCA     672
Glu Glu Ala Ala Asp Trp Asp Arg Thr His Pro Val Pro Val Gly Pro
    210                 215                 220
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CTA CCC CCA GGG CAA CTG AGA GAC CCT AGA GGA AGT GAT ATA GCA GGA     720
Leu Pro Pro Gly Gln Leu Arg Asp Pro Arg Gly Ser Asp Ile Ala Gly
225                 230                 235                 240

ACA ACT AGC ACC CTG GCA GAA CAG GTG GCT TGG ATG ACT GCT AAT CCT     768
Thr Thr Ser Thr Leu Ala Glu Gln Val Ala Trp Met Thr Ala Asn Pro
                245                 250                 255

CCT GTT CCA GTA GGA GAT ATT TAT AGA AGA TGG ATA GTC CTG GGG TTA     816
Pro Val Pro Val Gly Asp Ile Tyr Arg Arg Trp Ile Val Leu Gly Leu
            260                 265                 270

AAC AGA ATT GTG AGA ATG TAT AGT CCT GTC AGC ATT CTA GAG ATC AAA     864
Asn Arg Ile Val Arg Met Tyr Ser Pro Val Ser Ile Leu Glu Ile Lys
        275                 280                 285

CAA GGA CCA AAA GAA CCC TTC AGA GAC TAT GTA GAC AGG TTC TAC AAA     912
Gln Gly Pro Lys Glu Pro Phe Arg Asp Tyr Val Asp Arg Phe Tyr Lys
    290                 295                 300

ACT CTA AGA GCA GAG CAG GCA ACA CAG GAA GTA AAG AAT TGG ATG ACA     960
Thr Leu Arg Ala Glu Gln Ala Thr Gln Glu Val Lys Asn Trp Met Thr
305                 310                 315                 320

GAA ACA CTC TTA GTA CAA AAT GCA AAC CCA GAT TGT AAA CAG CTC CTA    1008
Glu Thr Leu Leu Val Gln Asn Ala Asn Pro Asp Cys Lys Gln Leu Leu
                325                 330                 335

AAA GCA TTA GGG CCA GGA GCT ACC TTA GAA GAG ATG ATG ACG GCC TGC    1056
Lys Ala Leu Gly Pro Gly Ala Thr Leu Glu Glu Met Met Thr Ala Cys
            340                 345                 350

CAG GGA GTG GGG GGA CCA GCA CAT AAG GCA AGA GTG CTA GCA GAG GCT    1104
Gln Gly Val Gly Gly Pro Ala His Lys Ala Arg Val Leu Ala Glu Ala
        355                 360                 365

ATG TCA CAG GTG CAG CAG CCA ACA ACT AGT GTC TTT GCA CAA AGG GGA    1152
Met Ser Gln Val Gln Gln Pro Thr Thr Ser Val Phe Ala Gln Arg Gly
    370                 375                 380

AAC TTT AAA GGC ATA AGG AAA CCC ATT AAA TGT TTC AAT TGT GGC AAA    1200
Asn Phe Lys Gly Ile Arg Lys Pro Ile Lys Cys Phe Asn Cys Gly Lys
385                 390                 395                 400

GAG GGC CAT TTG GCA AGA AAC TGT AAG GCC CCT AGA AGA GGA GGC TGT    1248
Glu Gly His Leu Ala Arg Asn Cys Lys Ala Pro Arg Arg Gly Gly Cys
                405                 410                 415

TGG AAG TGT GGG CAA GAA GGA CAT CAA ATG AAA GAT TGT AAA AAT GAA    1296
Trp Lys Cys Gly Gln Glu Gly His Gln Met Lys Asp Cys Lys Asn Glu
            420                 425                 430

GGA AGA CAG GCT AAT TTT TTA GGG AAG AGC TGG TCT CCC TTC AAA GGG    1344
Gly Arg Gln Ala Asn Phe Leu Gly Lys Ser Trp Ser Pro Phe Lys Gly
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        435                 440                 445

AGA CCA GGA AAC TTC CCC CAG ACA ACA ACA AGG AAA GAG CCC ACA GCC   1392
Arg Pro Gly Asn Phe Pro Gln Thr Thr Thr Arg Lys Glu Pro Thr Ala
    450                 455                 460

CCG CCA CTA GAG AGT TAT GGG TTT CAG GAG GAG AAG AGC ACA CAG GGG   1440
Pro Pro Leu Glu Ser Tyr Gly Phe Gln Glu Glu Lys Ser Thr Gln Gly
465                 470                 475                 480

AAG GAG ATG CAG GAG AAC CAG GAG AGG ACA GAG AAC TCT CTG TAC CCA   1488
Lys Glu Met Gln Glu Asn Gln Glu Arg Thr Glu Asn Ser Leu Tyr Pro
                485                 490                 495

CCT TTA ACT TCC CTC AGA TCA CTC TTT GGC AAC GAC CCG TCA TCA CAG   1536
Pro Leu Thr Ser Leu Arg Ser Leu Phe Gly Asn Asp Pro Ser Ser Gln
            500                 505                 510

TAA                                                              1539
```

(2) INFORMATION FOR SEQ ID NO: 4:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 512 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 4:

```
Met Gly Ala Arg Ala Ser Val Leu Thr Gly Gly Lys Leu Asp Gln Trp
 1               5                  10                  15

Glu Ser Ile Tyr Leu Arg Pro Gly Gly Lys Lys Lys Tyr Arg Met Lys
            20                  25                  30

His Leu Val Trp Ala Ser Arg Glu Leu Glu Arg Phe Ala Cys Asn Pro
        35                  40                  45

Gly Leu Met Asp Thr Ala Asp Gly Cys Ala Lys Leu Leu Asn Gln Leu
    50                  55                  60

Glu Pro Ala Leu Lys Thr Gly Ser Glu Glu Leu Arg Ser Leu Tyr Asn
65                  70                  75                  80

Ala Leu Ala Val Leu Tyr Cys Val His Ser Arg Ile Gln Ile His Asn
                85                  90                  95

Thr Gln Glu Ala Leu Asp Lys Ile Lys Glu Lys Gln Glu Gln His Lys
            100                 105                 110

Pro Glu Pro Lys Asn Pro Glu Ala Gly Ala Ala Ala Ala Thr Asp Ser
        115                 120                 125
```

Asn Ile Ser Arg Asn Tyr Pro Leu Val Gln Thr Ala Gln Gly Gln Met
130 135 140

Val His Gln Pro Leu Thr Pro Arg Thr Leu Asn Ala Trp Val Lys Val
145 150 155 160

Ile Glu Glu Lys Ala Phe Ser Pro Glu Val Ile Pro Met Phe Met Ala
165 170 175

Leu Ser Glu Gly Ala Thr Pro Ser Asp Leu Asn Thr Met Leu Asn Thr
180 185 190

Val Gly Gly His Gln Ala Ala Met Gln Met Leu Lys Glu Val Ile Asn
195 200 205

Glu Glu Ala Ala Asp Trp Asp Arg Thr His Pro Val Pro Val Gly Pro
210 215 220

Leu Pro Pro Gly Gln Leu Arg Asp Pro Arg Gly Ser Asp Ile Ala Gly
225 230 235 240

Thr Thr Ser Thr Leu Ala Glu Gln Val Ala Trp Met Thr Ala Asn Pro
245 250 255

Pro Val Pro Val Gly Asp Ile Tyr Arg Arg Trp Ile Val Leu Gly Leu
260 265 270

Asn Arg Ile Val Arg Met Tyr Ser Pro Val Ser Ile Leu Glu Ile Lys
275 280 285

Gln Gly Pro Lys Glu Pro Phe Arg Asp Tyr Val Asp Arg Phe Tyr Lys
290 295 300

Thr Leu Arg Ala Glu Gln Ala Thr Gln Glu Val Lys Asn Trp Met Thr
305 310 315 320

Glu Thr Leu Leu Val Gln Asn Ala Asn Pro Asp Cys Lys Gln Leu Leu
325 330 335

Lys Ala Leu Gly Pro Gly Ala Thr Leu Glu Glu Met Met Thr Ala Cys
340 345 350

Gln Gly Val Gly Gly Pro Ala His Lys Ala Arg Val Leu Ala Glu Ala
355 360 365

Met Ser Gln Val Gln Gln Pro Thr Thr Ser Val Phe Ala Gln Arg Gly
370 375 380

Asn Phe Lys Gly Ile Arg Lys Pro Ile Lys Cys Phe Asn Cys Gly Lys
385 390 395 400

Glu Gly His Leu Ala Arg Asn Cys Lys Ala Pro Arg Arg Gly Gly Cys
405 410 415

Trp Lys Cys Gly Gln Glu Gly His Gln Met Lys Asp Cys Lys Asn Glu

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            420                 425                 430

Gly Arg Gln Ala Asn Phe Leu Gly Lys Ser Trp Ser Pro Phe Lys Gly
        435                 440                 445

Arg Pro Gly Asn Phe Pro Gln Thr Thr Thr Arg Lys Glu Pro Thr Ala
    450                 455                 460

Pro Pro Leu Glu Ser Tyr Gly Phe Gln Glu Glu Lys Ser Thr Gln Gly
465                 470                 475                 480

Lys Glu Met Gln Glu Asn Gln Glu Arg Thr Glu Asn Ser Leu Tyr Pro
                485                 490                 495

Pro Leu Thr Ser Leu Arg Ser Leu Phe Gly Asn Asp Pro Ser Ser Gln
            500                 505                 510
```

(2) INFORMATION FOR SEQ ID NO: 5:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 3045 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: ADN (genomic)

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION:1..3042

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 5:

```
TTT TTT AGG GAA GAG CTG GTC TCC CTT CAA AGG GAG ACC AGG AAA CTT      48
Phe Phe Arg Glu Glu Leu Val Ser Leu Gln Arg Glu Thr Arg Lys Leu
        515                 520                 525

CCC CCA GAC AAC AAC AAG GAA AGA GCC CAC AGC CCC GCC ACT AGA GAG      96
Pro Pro Asp Asn Asn Lys Glu Arg Ala His Ser Pro Ala Thr Arg Glu
    530                 535                 540

TTA TGG GTT TCA GGA GGA GAA GAG CAC ACA GGG GAA GGA GAT GCA GGA     144
Leu Trp Val Ser Gly Gly Glu Glu His Thr Gly Glu Gly Asp Ala Gly
545                 550                 555                 560

GAA CCA GGA GAG GAC AGA GAA CTC TCT GTA CCC ACC TTT AAC TTC CCT     192
Glu Pro Gly Glu Asp Arg Glu Leu Ser Val Pro Thr Phe Asn Phe Pro
                565                 570                 575

CAG ATC ACT CTT TGG CAA CGA CCC GTC ATC ACA GTA AAA ATA GGG AAA     240
Gln Ile Thr Leu Trp Gln Arg Pro Val Ile Thr Val Lys Ile Gly Lys
            580                 585                 590
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GAA GTA AGA GAA GCT CTT TTA GAT ACA GGA GCT GAT GAT ACA GTA ATA     288
Glu Val Arg Glu Ala Leu Leu Asp Thr Gly Ala Asp Asp Thr Val Ile
        595                 600                 605

GAA GAG CTA CAA TTA GAG GGA AAA TGG AAA CCA AAA ATG ATA GGA GGA     336
Glu Glu Leu Gln Leu Glu Gly Lys Trp Lys Pro Lys Met Ile Gly Gly
    610                 615                 620

ATT GGA GGA TTT ATC AAA GTG AGA CAA TAT GAT AAT ATA ACA GTA GAC     384
Ile Gly Gly Phe Ile Lys Val Arg Gln Tyr Asp Asn Ile Thr Val Asp
625                 630                 635                 640

ATA CAG GGA AGA AAA GCA GTT GGT ACA GTA TTA GTA GGA CCA ACA CCT     432
Ile Gln Gly Arg Lys Ala Val Gly Thr Val Leu Val Gly Pro Thr Pro
                645                 650                 655

GTT AAT ATT ATA GGA AGA AAT CTT TTA ACC CAG ATT GGC TGT ACT TTA     480
Val Asn Ile Ile Gly Arg Asn Leu Leu Thr Gln Ile Gly Cys Thr Leu
            660                 665                 670

AAT TTT CCA ATA AGT CCT ATT GAA ACT GTA CCA GTA AAA TTA AAA CCA     528
Asn Phe Pro Ile Ser Pro Ile Glu Thr Val Pro Val Lys Leu Lys Pro
        675                 680                 685

GGA ATG GAT GGC CCA AAG GTA AAA CAA TGG CCT TTG ACA ACA GAA AAA     576
Gly Met Asp Gly Pro Lys Val Lys Gln Trp Pro Leu Thr Thr Glu Lys
    690                 695                 700

ATA GAG GCA TTA AGA GAA ATT TGT ACA GAA ATG GAA AAG GAA GGA AAA     624
Ile Glu Ala Leu Arg Glu Ile Cys Thr Glu Met Glu Lys Glu Gly Lys
705                 710                 715                 720

ATT TCT AGA ATA GGG CCT GAG AAT CCA TAT AAC ACT CCA ATT TTT GCT     672
Ile Ser Arg Ile Gly Pro Glu Asn Pro Tyr Asn Thr Pro Ile Phe Ala
                725                 730                 735

ATA AAA AAG AAA GAT AGC ACT AAA TGG AGA AAA TTA GTA GAT TTC AGG     720
Ile Lys Lys Lys Asp Ser Thr Lys Trp Arg Lys Leu Val Asp Phe Arg
            740                 745                 750

GAA TTA AAT AAA AGG ACC CAA GAT TTT TGG GAA GTG CAG CTA GGA ATT     768
Glu Leu Asn Lys Arg Thr Gln Asp Phe Trp Glu Val Gln Leu Gly Ile
        755                 760                 765

CCA CAT CCA GCA GGA TTA AAG CAG AAA AAA TCA GTG ACA GTT TTG GAT     816
Pro His Pro Ala Gly Leu Lys Gln Lys Lys Ser Val Thr Val Leu Asp
    770                 775                 780

GTA GGA GAT GCT TAT TTT TCA TGT CCC TTG GAC AAA GAT TTT AGA AAG     864
Val Gly Asp Ala Tyr Phe Ser Cys Pro Leu Asp Lys Asp Phe Arg Lys
785                 790                 795                 800

TAT ACA GCT TTT ACC ATA CCT AGT ATA AAC AAT GAG ACA CCT GGT ATT     912
Tyr Thr Ala Phe Thr Ile Pro Ser Ile Asn Asn Glu Thr Pro Gly Ile
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                805                 810                 815

AGA TAC CAG TAT AAT GTG CTG CCA CAA GGC TGG AAA GGG TCA CCA GCA     960
Arg Tyr Gln Tyr Asn Val Leu Pro Gln Gly Trp Lys Gly Ser Pro Ala
            820                 825                 830

ATT TTT CAG AGT ACA ATG ACA AAA ATT CTA GAA CCA TTC AGA GAG AAA    1008
Ile Phe Gln Ser Thr Met Thr Lys Ile Leu Glu Pro Phe Arg Glu Lys
        835                 840                 845

CAT CCA GAG ATA ATC ATT TAC CAG TAC ATG GAT GAC CTC TAT GTG GGA    1056
His Pro Glu Ile Ile Ile Tyr Gln Tyr Met Asp Asp Leu Tyr Val Gly
    850                 855                 860

TCT GAC TTA GAA CTA GCA CAA CAT AGA GAG GCA GTA GAA GAC CTC AGA    1104
Ser Asp Leu Glu Leu Ala Gln His Arg Glu Ala Val Glu Asp Leu Arg
865                 870                 875                 880

GAT CAT CTT TTG AAG TGG GGC TTT ACG ACC CCT GAC AAA AAA CAT CAG    1152
Asp His Leu Leu Lys Trp Gly Phe Thr Thr Pro Asp Lys Lys His Gln
                885                 890                 895

AAG GAG CCC CCG TTC CTC TGG ATG GGA TAT GAA CTC CAT CCA GAC AAA    1200
Lys Glu Pro Pro Phe Leu Trp Met Gly Tyr Glu Leu His Pro Asp Lys
            900                 905                 910

TGG ACA GTC CAG CCA ATA AAG TTA CCA GAA AAG GAT GTA TGG ACT GTC    1248
Trp Thr Val Gln Pro Ile Lys Leu Pro Glu Lys Asp Val Trp Thr Val
        915                 920                 925

AAT GAT ATA CAG AAA TTA GTA GGA AAG TTA AAT TGG GCA AGT CAG ATC    1296
Asn Asp Ile Gln Lys Leu Val Gly Lys Leu Asn Trp Ala Ser Gln Ile
    930                 935                 940

TAT CCA GGA ATC AGA GTA AAA CAG CTC TGT AAA TTA ATC AGA GGA GCC    1344
Tyr Pro Gly Ile Arg Val Lys Gln Leu Cys Lys Leu Ile Arg Gly Ala
945                 950                 955                 960

AGA GCT TTG ACA GAA GTA GTC AAC TTT ACA GAA GAA GCA GAA TTA GAA    1392
Arg Ala Leu Thr Glu Val Val Asn Phe Thr Glu Glu Ala Glu Leu Glu
                965                 970                 975

CTA GCA GAA AAC AGG GAG ATA TTA AAA GAA CCC CTG CAT GGA GTC TAT    1440
Leu Ala Glu Asn Arg Glu Ile Leu Lys Glu Pro Leu His Gly Val Tyr
            980                 985                 990

TAT GAC CCA GGA AAA GAA TTA GTA GCA GAA ATT CAA AAG CAA GGA CAA    1488
Tyr Asp Pro Gly Lys Glu Leu Val Ala Glu Ile Gln Lys Gln Gly Gln
        995                 1000                1005

GGT CAG TGG ACA TAT CAG ATT TAT CAG GAG TTA CAT AAA AAT TTA AAA    1536
Gly Gln Trp Thr Tyr Gln Ile Tyr Gln Glu Leu His Lys Asn Leu Lys
    1010                1015                1020

ACA GGA AAG TAT GCA AAA ATG AGA TCT GCC CAT ACT AAT GAT ATA AAA    1584
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Thr Gly Lys Tyr Ala Lys Met Arg Ser Ala His Thr Asn Asp Ile Lys
1025                1030                1035                1040

CAG TTA GTT GAA GTG GTA AGG AAA GTG GCA ACA GAA AGT ATA GTA ATT   1632
Gln Leu Val Glu Val Val Arg Lys Val Ala Thr Glu Ser Ile Val Ile
                1045                1050                1055

TGG GGA AAG ACT CCT AAA TTT AGA TTA CCA GTA CAA AAG GAA GTG TGG   1680
Trp Gly Lys Thr Pro Lys Phe Arg Leu Pro Val Gln Lys Glu Val Trp
            1060                1065                1070

GAG GCA TGG TGG ACC GAT CAT TGG CAA GCA ACT TGG ATT CCT GAG TGG   1728
Glu Ala Trp Trp Thr Asp His Trp Gln Ala Thr Trp Ile Pro Glu Trp
        1075                1080                1085

GAA TTT GTC AAC ACT CCT CCC CTT GTA AAA TTA TGG TAT CAG TTA GAA   1776
Glu Phe Val Asn Thr Pro Pro Leu Val Lys Leu Trp Tyr Gln Leu Glu
    1090                1095                1100

ACA GAG CCA ATC AGT GGG GCA GAA ACT TTC TAT GTA GAT GGA GCA GCT   1824
Thr Glu Pro Ile Ser Gly Ala Glu Thr Phe Tyr Val Asp Gly Ala Ala
1105                1110                1115                1120

AAT AGG GAA ACA AAA TTG GGA AAA GCA GGT TTT GTG ACA GAT AGG GGA   1872
Asn Arg Glu Thr Lys Leu Gly Lys Ala Gly Phe Val Thr Asp Arg Gly
                1125                1130                1135

AGA CAG AAA GTG GTC TCT ATT GCA GAC ACC ACC AAT CAA AAG GCT GAG   1920
Arg Gln Lys Val Val Ser Ile Ala Asp Thr Thr Asn Gln Lys Ala Glu
            1140                1145                1150

TTA CAA GCT ATC CTT ATG GCC TTA CAA GAG TCA GGA CGG GAT GTA AAC   1968
Leu Gln Ala Ile Leu Met Ala Leu Gln Glu Ser Gly Arg Asp Val Asn
        1155                1160                1165

ATA GTC ACT GAC TCT CAG TAT GCT ATG GGA ATA ATT CAT TCA CAG CCA   2016
Ile Val Thr Asp Ser Gln Tyr Ala Met Gly Ile Ile His Ser Gln Pro
    1170                1175                1180

GAT AAA AGT GAA TCA GAA TTG GTG AGC CAA ATA ATA GAA GAG CTC ATA   2064
Asp Lys Ser Glu Ser Glu Leu Val Ser Gln Ile Ile Glu Glu Leu Ile
1185                1190                1195                1200

AAA AAG GAA AGA GTT TAT CTC TCT TGG GTA CCT GCA CAT AAA GGT ATT   2112
Lys Lys Glu Arg Val Tyr Leu Ser Trp Val Pro Ala His Lys Gly Ile
                1205                1210                1215

GGA GGA AAT GAG CAG GTA GAC AAA TTA GTT AGC TCA GGA ATT AGA AAA   2160
Gly Gly Asn Glu Gln Val Asp Lys Leu Val Ser Ser Gly Ile Arg Lys
            1220                1225                1230

ATA TTA TTC CTA GAT GGT ATA GAA AAA GCC CAA GAA GAT CAT GAC AGA   2208
Ile Leu Phe Leu Asp Gly Ile Glu Lys Ala Gln Glu Asp His Asp Arg
        1235                1240                1245
```

```
TAT CAC AGC AAT TGG AAA GCA ATG GCC AGT GAT TTT AAC TTA CCC CCC   2256
Tyr His Ser Asn Trp Lys Ala Met Ala Ser Asp Phe Asn Leu Pro Pro
    1250                1255                1260

ATA GTG GCA AAA GAA ATA GTA GCC AGC TGT GAC AAA TGC CAG CTA AAA   2304
Ile Val Ala Lys Glu Ile Val Ala Ser Cys Asp Lys Cys Gln Leu Lys
1265                1270                1275                1280

GGG GAA GCC ATG CAT GGA CAG GTC AAT TGT AGT CCA GGA GTG TGG CAA   2352
Gly Glu Ala Met His Gly Gln Val Asn Cys Ser Pro Gly Val Trp Gln
                1285                1290                1295

TTA GAT TGT ACA CAC TTA GAG GGA AAA ATC ATC CTT GTG GCG GTC CAT   2400
Leu Asp Cys Thr His Leu Glu Gly Lys Ile Ile Leu Val Ala Val His
            1300                1305                1310

GTG GCC AGT GGC TAC TTA GAA GCA GAA GTT ATT CCT GCA GAG ACA GGA   2448
Val Ala Ser Gly Tyr Leu Glu Ala Glu Val Ile Pro Ala Glu Thr Gly
        1315                1320                1325

CAG GAA ACA GCA TAT TTT ATT TTA AAG TTA GCT GGA AGA TGG CCA GTA   2496
Gln Glu Thr Ala Tyr Phe Ile Leu Lys Leu Ala Gly Arg Trp Pro Val
    1330                1335                1340

AAA GTT ATA CAC ACT GAT AAT GGA TCC AAT TTC ACT AGT GCC ACT GTA   2544
Lys Val Ile His Thr Asp Asn Gly Ser Asn Phe Thr Ser Ala Thr Val
1345                1350                1355                1360

AAA GCA GCC TGT TGG TGG GCA AAT ATC AAA CAG GAA TTT GGG ATA CCC   2592
Lys Ala Ala Cys Trp Trp Ala Asn Ile Lys Gln Glu Phe Gly Ile Pro
                1365                1370                1375

TAC AAT CCT CAA AGT CAG GGA GCA GTA GAG TCC ATG AAT AAA GAA TTA   2640
Tyr Asn Pro Gln Ser Gln Gly Ala Val Glu Ser Met Asn Lys Glu Leu
            1380                1385                1390

AAG AAA ATT ATA GGA CAA ATC AGA GAT CAA GCA GAA CAT CTA AAG ACA   2688
Lys Lys Ile Ile Gly Gln Ile Arg Asp Gln Ala Glu His Leu Lys Thr
        1395                1400                1405

GCA GTG CAA ATG GCG GTT TTC ATT CAC AAT TTT AAA AGA AAA GGG GGG   2736
Ala Val Gln Met Ala Val Phe Ile His Asn Phe Lys Arg Lys Gly Gly
    1410                1415                1420

ATT GGG GGG TAC ACT GCA GGG GAA AGA ATA ATA GAC ATA ATA GCA ACA   2784
Ile Gly Gly Tyr Thr Ala Gly Glu Arg Ile Ile Asp Ile Ile Ala Thr
1425                1430                1435                1440

GAC ATA CAG ACA ACA AAT TTA CAA ACA CAA ATT TTA AAA GTT CAA AAT   2832
Asp Ile Gln Thr Thr Asn Leu Gln Thr Gln Ile Leu Lys Val Gln Asn
                1445                1450                1455

TTT CGG GTT TAT TAC AGA GAC AGC AGA GAT CCC ATT TGG AAA GGA CCA   2880
Phe Arg Val Tyr Tyr Arg Asp Ser Arg Asp Pro Ile Trp Lys Gly Pro
            1460                1465                1470
```

```
GCC AAA CTT CTG TGG AAA GGA GAA GGG GCA GTG GTA ATT CAA GAT AAC   2928
Ala Lys Leu Leu Trp Lys Gly Glu Gly Ala Val Val Ile Gln Asp Asn
        1475                1480                1485

GGG GAT ATA AAA GTA GTC CCA CGT AGG AAA GCA AAA ATA ATT AGG GAT   2976
Gly Asp Ile Lys Val Val Pro Arg Arg Lys Ala Lys Ile Ile Arg Asp
    1490                1495                1500

TAT GGA AAA CAG ATG GCA GGT GAT GGT TGT GTG GCA AGT GGA CAG GAT   3024
Tyr Gly Lys Gln Met Ala Gly Asp Gly Cys Val Ala Ser Gly Gln Asp
1505                1510                1515                1520

GAA AAT CAG GAA ATG GAA TAG                                      3045
Glu Asn Gln Glu Met Glu
                1525
```

(2) INFORMATION FOR SEQ ID NO: 6:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 1014 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 6:

```
Phe Phe Arg Glu Glu Leu Val Ser Leu Gln Arg Glu Thr Arg Lys Leu
 1               5                  10                  15

Pro Pro Asp Asn Asn Lys Glu Arg Ala His Ser Pro Ala Thr Arg Glu
            20                  25                  30

Leu Trp Val Ser Gly Gly Glu Glu His Thr Gly Glu Gly Asp Ala Gly
        35                  40                  45

Glu Pro Gly Glu Asp Arg Glu Leu Ser Val Pro Thr Phe Asn Phe Pro
    50                  55                  60

Gln Ile Thr Leu Trp Gln Arg Pro Val Ile Thr Val Lys Ile Gly Lys
65                  70                  75                  80

Glu Val Arg Glu Ala Leu Leu Asp Thr Gly Ala Asp Asp Thr Val Ile
                85                  90                  95

Glu Glu Leu Gln Leu Glu Gly Lys Trp Lys Pro Lys Met Ile Gly Gly
            100                 105                 110

Ile Gly Gly Phe Ile Lys Val Arg Gln Tyr Asp Asn Ile Thr Val Asp
        115                 120                 125

Ile Gln Gly Arg Lys Ala Val Gly Thr Val Leu Val Gly Pro Thr Pro
    130                 135                 140
```

Val Asn Ile Ile Gly Arg Asn Leu Leu Thr Gln Ile Gly Cys Thr Leu
145 150 155 160

Asn Phe Pro Ile Ser Pro Ile Glu Thr Val Pro Val Lys Leu Lys Pro
165 170 175

Gly Met Asp Gly Pro Lys Val Lys Gln Trp Pro Leu Thr Thr Glu Lys
180 185 190

Ile Glu Ala Leu Arg Glu Ile Cys Thr Glu Met Glu Lys Glu Gly Lys
195 200 205

Ile Ser Arg Ile Gly Pro Glu Asn Pro Tyr Asn Thr Pro Ile Phe Ala
210 215 220

Ile Lys Lys Lys Asp Ser Thr Lys Trp Arg Lys Leu Val Asp Phe Arg
225 230 235 240

Glu Leu Asn Lys Arg Thr Gln Asp Phe Trp Glu Val Gln Leu Gly Ile
245 250 255

Pro His Pro Ala Gly Leu Lys Gln Lys Lys Ser Val Thr Val Leu Asp
260 265 270

Val Gly Asp Ala Tyr Phe Ser Cys Pro Leu Asp Lys Asp Phe Arg Lys
275 280 285

Tyr Thr Ala Phe Thr Ile Pro Ser Ile Asn Asn Glu Thr Pro Gly Ile
290 295 300

Arg Tyr Gln Tyr Asn Val Leu Pro Gln Gly Trp Lys Gly Ser Pro Ala
305 310 315 320

Ile Phe Gln Ser Thr Met Thr Lys Ile Leu Glu Pro Phe Arg Glu Lys
325 330 335

His Pro Glu Ile Ile Ile Tyr Gln Tyr Met Asp Asp Leu Tyr Val Gly
340 345 350

Ser Asp Leu Glu Leu Ala Gln His Arg Glu Ala Val Glu Asp Leu Arg
355 360 365

Asp His Leu Leu Lys Trp Gly Phe Thr Thr Pro Asp Lys Lys His Gln
370 375 380

Lys Glu Pro Pro Phe Leu Trp Met Gly Tyr Glu Leu His Pro Asp Lys
385 390 395 400

Trp Thr Val Gln Pro Ile Lys Leu Pro Glu Lys Asp Val Trp Thr Val
405 410 415

Asn Asp Ile Gln Lys Leu Val Gly Lys Leu Asn Trp Ala Ser Gln Ile
420 425 430

Tyr Pro Gly Ile Arg Val Lys Gln Leu Cys Lys Leu Ile Arg Gly Ala

435 440 445

Arg Ala Leu Thr Glu Val Val Asn Phe Thr Glu Glu Ala Glu Leu Glu
450 455 460

Leu Ala Glu Asn Arg Glu Ile Leu Lys Glu Pro Leu His Gly Val Tyr
465 470 475 480

Tyr Asp Pro Gly Lys Glu Leu Val Ala Glu Ile Gln Lys Gln Gly Gln
485 490 495

Gly Gln Trp Thr Tyr Gln Ile Tyr Gln Glu Leu His Lys Asn Leu Lys
500 505 510

Thr Gly Lys Tyr Ala Lys Met Arg Ser Ala His Thr Asn Asp Ile Lys
515 520 525

Gln Leu Val Glu Val Val Arg Lys Val Ala Thr Glu Ser Ile Val Ile
530 535 540

Trp Gly Lys Thr Pro Lys Phe Arg Leu Pro Val Gln Lys Glu Val Trp
545 550 555 560

Glu Ala Trp Trp Thr Asp His Trp Gln Ala Thr Trp Ile Pro Glu Trp
565 570 575

Glu Phe Val Asn Thr Pro Pro Leu Val Lys Leu Trp Tyr Gln Leu Glu
580 585 590

Thr Glu Pro Ile Ser Gly Ala Glu Thr Phe Tyr Val Asp Gly Ala Ala
595 600 605

Asn Arg Glu Thr Lys Leu Gly Lys Ala Gly Phe Val Thr Asp Arg Gly
610 615 620

Arg Gln Lys Val Val Ser Ile Ala Asp Thr Thr Asn Gln Lys Ala Glu
625 630 635 640

Leu Gln Ala Ile Leu Met Ala Leu Gln Glu Ser Gly Arg Asp Val Asn
645 650 655

Ile Val Thr Asp Ser Gln Tyr Ala Met Gly Ile Ile His Ser Gln Pro
660 665 670

Asp Lys Ser Glu Ser Glu Leu Val Ser Gln Ile Ile Glu Glu Leu Ile
675 680 685

Lys Lys Glu Arg Val Tyr Leu Ser Trp Val Pro Ala His Lys Gly Ile
690 695 700

Gly Gly Asn Glu Gln Val Asp Lys Leu Val Ser Ser Gly Ile Arg Lys
705 710 715 720

Ile Leu Phe Leu Asp Gly Ile Glu Lys Ala Gln Glu Asp His Asp Arg
725 730 735

```
Tyr His Ser Asn Trp Lys Ala Met Ala Ser Asp Phe Asn Leu Pro Pro
            740                 745                 750

Ile Val Ala Lys Glu Ile Val Ala Ser Cys Asp Lys Cys Gln Leu Lys
        755                 760                 765

Gly Glu Ala Met His Gly Gln Val Asn Cys Ser Pro Gly Val Trp Gln
    770                 775                 780

Leu Asp Cys Thr His Leu Glu Gly Lys Ile Ile Leu Val Ala Val His
785                 790                 795                 800

Val Ala Ser Gly Tyr Leu Glu Ala Glu Val Ile Pro Ala Glu Thr Gly
                805                 810                 815

Gln Glu Thr Ala Tyr Phe Ile Leu Lys Leu Ala Gly Arg Trp Pro Val
            820                 825                 830

Lys Val Ile His Thr Asp Asn Gly Ser Asn Phe Thr Ser Ala Thr Val
        835                 840                 845

Lys Ala Ala Cys Trp Trp Ala Asn Ile Lys Gln Glu Phe Gly Ile Pro
    850                 855                 860

Tyr Asn Pro Gln Ser Gln Gly Ala Val Glu Ser Met Asn Lys Glu Leu
865                 870                 875                 880

Lys Lys Ile Ile Gly Gln Ile Arg Asp Gln Ala Glu His Leu Lys Thr
                885                 890                 895

Ala Val Gln Met Ala Val Phe Ile His Asn Phe Lys Arg Lys Gly Gly
            900                 905                 910

Ile Gly Gly Tyr Thr Ala Gly Glu Arg Ile Ile Asp Ile Ile Ala Thr
        915                 920                 925

Asp Ile Gln Thr Thr Asn Leu Gln Thr Gln Ile Leu Lys Val Gln Asn
    930                 935                 940

Phe Arg Val Tyr Tyr Arg Asp Ser Arg Asp Pro Ile Trp Lys Gly Pro
945                 950                 955                 960

Ala Lys Leu Leu Trp Lys Gly Glu Gly Ala Val Val Ile Gln Asp Asn
                965                 970                 975

Gly Asp Ile Lys Val Val Pro Arg Arg Lys Ala Lys Ile Ile Arg Asp
            980                 985                 990

Tyr Gly Lys Gln Met Ala Gly Asp Gly Cys Val Ala Ser Gly Gln Asp
        995                 1000                1005

Glu Asn Gln Glu Met Glu
    1010
```

(2) INFORMATION FOR SEQ ID NO: 7:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 579 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: ADN (genomic)

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION:1..576

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 7:

```
ATG GAA AAC AGA TGG CAG GTG ATG GTT GTG TGG CAA GTG GAC AGG ATG     48
Met Glu Asn Arg Trp Gln Val Met Val Val Trp Gln Val Asp Arg Met
1015                1020                1025                1030

AAA ATC AGG AAA TGG AAT AGC TTA GTA AAA CAT CAT ATG TAT GTG TCA     96
Lys Ile Arg Lys Trp Asn Ser Leu Val Lys His His Met Tyr Val Ser
                1035                1040                1045

AAA AAG GCA AAA GGA TGG TAT TAT AGA CAT CAT TAT GAA ACA CAT CAC    144
Lys Lys Ala Lys Gly Trp Tyr Tyr Arg His His Tyr Glu Thr His His
            1050                1055                1060

CCA AAA ATA AGT TCA GAA GTA CAT ATC CCA GTA GGT CAG GCA AGA TTA    192
Pro Lys Ile Ser Ser Glu Val His Ile Pro Val Gly Gln Ala Arg Leu
        1065                1070                1075

GTG ACA GTC ACT TAT TGG GGG CTA ACA ACA GGA GAA CAG TCT TGG CAT    240
Val Thr Val Thr Tyr Trp Gly Leu Thr Thr Gly Glu Gln Ser Trp His
    1080                1085                1090

CTA GGA CAT GGA GTA TCC ATA GAA TGG AGA CTA AGA AAA TAC AAG ACA    288
Leu Gly His Gly Val Ser Ile Glu Trp Arg Leu Arg Lys Tyr Lys Thr
1095                1100                1105                1110

CAA GTT GAT CCT GAA ATG GCA GAC AAG CTA ATA CAT CTT CAT TAT TTT    336
Gln Val Asp Pro Glu Met Ala Asp Lys Leu Ile His Leu His Tyr Phe
                1115                1120                1125

GAT TGT TTT ACA GCC TCT GCC ATA AGG CAA GCG GTC TTA GGG AGA CCA    384
Asp Cys Phe Thr Ala Ser Ala Ile Arg Gln Ala Val Leu Gly Arg Pro
            1130                1135                1140

GTA TTA CCT AGG TGT GAA TAT CCA GCA GGG CAC AAA CAG GTA GGC ACC    432
Val Leu Pro Arg Cys Glu Tyr Pro Ala Gly His Lys Gln Val Gly Thr
        1145                1150                1155

CTA CAA TAT CTA GCA CTA ACA GCC TGG GTG GGA GCA AAG AAG AGA AAG    480
Leu Gln Tyr Leu Ala Leu Thr Ala Trp Val Gly Ala Lys Lys Arg Lys
```

```
    1160                1165                1170

CCA CCC TTA CCT AGT GTG ACT AAG CTA ACA GAA GAT AGA TGG AAC GAG     528
Pro Pro Leu Pro Ser Val Thr Lys Leu Thr Glu Asp Arg Trp Asn Glu
1175                1180                1185                1190

CAC CAG AAG ATG CAG GGC CAC AGA GGG AAC CCT ATA ATG AAT GGG CAC     576
His Gln Lys Met Gln Gly His Arg Gly Asn Pro Ile Met Asn Gly His
            1195                1200                1205

TAG                                                                 579
```

(2) INFORMATION FOR SEQ ID NO: 8:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 192 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 8:

```
Met Glu Asn Arg Trp Gln Val Met Val Val Trp Gln Val Asp Arg Met
  1               5                  10                  15

Lys Ile Arg Lys Trp Asn Ser Leu Val Lys His His Met Tyr Val Ser
             20                  25                  30

Lys Lys Ala Lys Gly Trp Tyr Tyr Arg His His Tyr Glu Thr His His
         35                  40                  45

Pro Lys Ile Ser Ser Glu Val His Ile Pro Val Gly Gln Ala Arg Leu
     50                  55                  60

Val Thr Val Thr Tyr Trp Gly Leu Thr Thr Gly Glu Gln Ser Trp His
 65                  70                  75                  80

Leu Gly His Gly Val Ser Ile Glu Trp Arg Leu Arg Lys Tyr Lys Thr
                 85                  90                  95

Gln Val Asp Pro Glu Met Ala Asp Lys Leu Ile His Leu His Tyr Phe
            100                 105                 110

Asp Cys Phe Thr Ala Ser Ala Ile Arg Gln Ala Val Leu Gly Arg Pro
        115                 120                 125

Val Leu Pro Arg Cys Glu Tyr Pro Ala Gly His Lys Gln Val Gly Thr
    130                 135                 140

Leu Gln Tyr Leu Ala Leu Thr Ala Trp Val Gly Ala Lys Lys Arg Lys
145                 150                 155                 160

Pro Pro Leu Pro Ser Val Thr Lys Leu Thr Glu Asp Arg Trp Asn Glu
                165                 170                 175
```

His Gln Lys Met Gln Gly His Arg Gly Asn Pro Ile Met Asn Gly His
180 185 190

(2) INFORMATION FOR SEQ ID NO: 9:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 288 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: ADN (genomic)

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION:1..285

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 9:

```
ATG GAA CGA GCA CCA GAA GAT GCA GGG CCA CAG AGG GAA CCC TAT AAT     48
Met Glu Arg Ala Pro Glu Asp Ala Gly Pro Gln Arg Glu Pro Tyr Asn
        195                 200                 205

GAA TGG GCA CTA GAA TTA TTA GAA GAA TTA AAA AAT GAA GCT GTG CGC     96
Glu Trp Ala Leu Glu Leu Leu Glu Glu Leu Lys Asn Glu Ala Val Arg
    210                 215                 220

CAT TTT CCA AGG ATT TGG CTA CAT GGG TTA GGA CAA CAC ATC TAT AAC    144
His Phe Pro Arg Ile Trp Leu His Gly Leu Gly Gln His Ile Tyr Asn
225                 230                 235                 240

ACA TAT GGA GAC ACC TGG GAG GGG GTA GAG GCA ATT ATC AGG ATA CTA    192
Thr Tyr Gly Asp Thr Trp Glu Gly Val Glu Ala Ile Ile Arg Ile Leu
                245                 250                 255

CAA CAA TTA CTG TTT ATC CAT TAT AGG ATT GGC TGC CAG CAC AGC AGA    240
Gln Gln Leu Leu Phe Ile His Tyr Arg Ile Gly Cys Gln His Ser Arg
            260                 265                 270

ATA GGG ATC ACT CCT CAA AGG AGA AGG AAT GGA ACC AGT AGA TCC        285
Ile Gly Ile Thr Pro Gln Arg Arg Arg Asn Gly Thr Ser Arg Ser
        275                 280                 285

TAG                                                                288
```

(2) INFORMATION FOR SEQ ID NO: 10:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 95 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 10:

```
Met Glu Arg Ala Pro Glu Asp Ala Gly Pro Gln Arg Glu Pro Tyr Asn
 1               5                  10                  15

Glu Trp Ala Leu Glu Leu Leu Glu Glu Leu Lys Asn Glu Ala Val Arg
            20                  25                  30

His Phe Pro Arg Ile Trp Leu His Gly Leu Gly Gln His Ile Tyr Asn
        35                  40                  45

Thr Tyr Gly Asp Thr Trp Glu Gly Val Glu Ala Ile Ile Arg Ile Leu
    50                  55                  60

Gln Gln Leu Leu Phe Ile His Tyr Arg Ile Gly Cys Gln His Ser Arg
65                  70                  75                  80

Ile Gly Ile Thr Pro Gln Arg Arg Arg Asn Gly Thr Ser Arg Ser
                85                  90                  95
```

(2) INFORMATION FOR SEQ ID NO: 11:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 252 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: ADN (genomic)

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION:1..249

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 11:

```
ATG CTG TCA TTG GGA TTC ATA GCG TTA GGA GCA GCA GTT AGC ATA GCA      48
Met Leu Ser Leu Gly Phe Ile Ala Leu Gly Ala Ala Val Ser Ile Ala
                100                 105                 110

GTA ATA GTC TGG GCA TTA CTA TAT AGA GAA TAT AAG AAA ATA AAA TTG      96
Val Ile Val Trp Ala Leu Leu Tyr Arg Glu Tyr Lys Lys Ile Lys Leu
            115                 120                 125

CAG GAA AAA ATA AAA CAC ATA AGA CAG AGA ATA AGA GAA AGA GAA GAA     144
Gln Glu Lys Ile Lys His Ile Arg Gln Arg Ile Arg Glu Arg Glu Glu
        130                 135                 140

GAT AGT GGC AAT GAA AGT GAT GGG GAT GCA GAG TGG TTG GAT GGG GAT     192
Asp Ser Gly Asn Glu Ser Asp Gly Asp Ala Glu Trp Leu Asp Gly Asp
    145                 150                 155
```

```
GAA GAG TGG TTG GTT ACT CTT CTA TCT TCT AGT AAG CTT GAT CAA GGT    240
Glu Glu Trp Leu Val Thr Leu Leu Ser Ser Ser Lys Leu Asp Gln Gly
160                 165                 170                 175

AAT TGG GTC TGA                                                252
Asn Trp Val
```

(2) INFORMATION FOR SEQ ID NO: 12:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 83 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 12:

```
Met Leu Ser Leu Gly Phe Ile Ala Leu Gly Ala Ala Val Ser Ile Ala
 1               5                  10                  15

Val Ile Val Trp Ala Leu Leu Tyr Arg Glu Tyr Lys Lys Ile Lys Leu
            20                  25                  30

Gln Glu Lys Ile Lys His Ile Arg Gln Arg Ile Arg Glu Arg Glu Glu
        35                  40                  45

Asp Ser Gly Asn Glu Ser Asp Gly Asp Ala Glu Trp Leu Asp Gly Asp
    50                  55                  60

Glu Glu Trp Leu Val Thr Leu Leu Ser Ser Ser Lys Leu Asp Gln Gly
65                  70                  75                  80

Asn Trp Val
```

(2) INFORMATION FOR SEQ ID NO: 13:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 306 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: ADN (genomic)

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION:1..303

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 13:

```
ATG GAA CCA GTA GAT CCT AGA TTA GAG CCC TGG AAT CAT CCA GGA AGC     48
```

```
Met Glu Pro Val Asp Pro Arg Leu Glu Pro Trp Asn His Pro Gly Ser
 85                  90                  95

CAA CCT AAA ACA GCT TGC AAT AAT TGC TAT TGT AAA AGA TGT TGC TAT      96
Gln Pro Lys Thr Ala Cys Asn Asn Cys Tyr Cys Lys Arg Cys Cys Tyr
100                 105                 110                 115

CAC TGC TTA TAT TGC TTC ACA AAG AAA GGC TTA GGC ATC TCA TAT GGC     144
His Cys Leu Tyr Cys Phe Thr Lys Lys Gly Leu Gly Ile Ser Tyr Gly
                120                 125                 130

AGG AAG AAG CGG AGT CAA CGA CGA AGA ACT CCT CAG AGC AGT AAG AGT     192
Arg Lys Lys Arg Ser Gln Arg Arg Arg Thr Pro Gln Ser Ser Lys Ser
            135                 140                 145

CAT CAA GAT CTT ATA CCA GAG CAG CCC TTA TCC CAA CAG CAA GGG GAC     240
His Gln Asp Leu Ile Pro Glu Gln Pro Leu Ser Gln Gln Gln Gly Asp
        150                 155                 160

CAG ACA GGC CAG AAG AAA CAG AAG GAG GCG TTG GAG AGC AAG ACA GAG     288
Gln Thr Gly Gln Lys Lys Gln Lys Glu Ala Leu Glu Ser Lys Thr Glu
    165                 170                 175

GCA GAT CCG TGC GAT TAG                                             306
Ala Asp Pro Cys Asp
180
```

(2) INFORMATION FOR SEQ ID NO: 14:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 101 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 14:

```
Met Glu Pro Val Asp Pro Arg Leu Glu Pro Trp Asn His Pro Gly Ser
 1               5                  10                  15

Gln Pro Lys Thr Ala Cys Asn Asn Cys Tyr Cys Lys Arg Cys Cys Tyr
            20                  25                  30

His Cys Leu Tyr Cys Phe Thr Lys Lys Gly Leu Gly Ile Ser Tyr Gly
        35                  40                  45

Arg Lys Lys Arg Ser Gln Arg Arg Arg Thr Pro Gln Ser Ser Lys Ser
    50                  55                  60

His Gln Asp Leu Ile Pro Glu Gln Pro Leu Ser Gln Gln Gln Gly Asp
65                  70                  75                  80

Gln Thr Gly Gln Lys Lys Gln Lys Glu Ala Leu Glu Ser Lys Thr Glu
                85                  90                  95
```

Ala Asp Pro Cys Asp
100

(2) INFORMATION FOR SEQ ID NO: 15:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 369 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: ADN (genomic)

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION:1..366

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 15:

```
ATG GCA GGA AGA AGC GGA GTC AAC GAC GAA GAA CTC CTC AGA GCA GTA      48
Met Ala Gly Arg Ser Gly Val Asn Asp Glu Glu Leu Leu Arg Ala Val
            105                 110                 115

AGA GTC ATC AAG ATC TTA TAC CAG AGC AGT TAT CCC AAC AGC AAG GGG      96
Arg Val Ile Lys Ile Leu Tyr Gln Ser Ser Tyr Pro Asn Ser Lys Gly
        120                 125                 130

ACC AGA CAG GCC AGA AGA AAC AGA AGG AGG CGT TGG AGA GCA AGA CAG     144
Thr Arg Gln Ala Arg Arg Asn Arg Arg Arg Arg Trp Arg Ala Arg Gln
    135                 140                 145

AGG CAG ATC CGT GCG ATT AGT GAG CGG ATT CTC AGC TCT TGT CTG GGA     192
Arg Gln Ile Arg Ala Ile Ser Glu Arg Ile Leu Ser Ser Cys Leu Gly
150                 155                 160                 165

GGA CCT CCG GAA CCT GTT GAT CTT CCT CTA CCA CCG CTT GAC AGA CTC     240
Gly Pro Pro Glu Pro Val Asp Leu Pro Leu Pro Pro Leu Asp Arg Leu
                170                 175                 180

ACT CTT GAT ACT GAG GAG GAC TCT GGA ACT CCT GGG ACA GAG TCT CAG     288
Thr Leu Asp Thr Glu Glu Asp Ser Gly Thr Pro Gly Thr Glu Ser Gln
            185                 190                 195

CAG GGG ACT GCA ACT ACT GAA TGA ACT CAG AAC ACA CTT GTG GGG AAT     336
Gln Gly Thr Ala Thr Thr Glu  *  Thr Gln Asn Thr Leu Val Gly Asn
        200                 205                 210

ACT TGC ATA TTG GGG AAA AGA GTT AAG GGA TAG                         369
Thr Cys Ile Leu Gly Lys Arg Val Lys Gly
    215                 220
```

(2) INFORMATION FOR SEQ ID NO: 16:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 122 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 16:

```
Met Ala Gly Arg Ser Gly Val Asn Asp Glu Glu Leu Leu Arg Ala Val
 1               5                  10                  15

Arg Val Ile Lys Ile Leu Tyr Gln Ser Ser Tyr Pro Asn Ser Lys Gly
            20                  25                  30

Thr Arg Gln Ala Arg Arg Asn Arg Arg Arg Arg Trp Arg Ala Arg Gln
        35                  40                  45

Arg Gln Ile Arg Ala Ile Ser Glu Arg Ile Leu Ser Ser Cys Leu Gly
    50                  55                  60

Gly Pro Pro Glu Pro Val Asp Leu Pro Leu Pro Pro Leu Asp Arg Leu
65                  70                  75                  80

Thr Leu Asp Thr Glu Glu Asp Ser Gly Thr Pro Gly Thr Glu Ser Gln
                85                  90                  95

Gln Gly Thr Ala Thr Thr Glu  *  Thr Gln Asn Thr Leu Val Gly Asn
            100                 105                 110

Thr Cys Ile Leu Gly Lys Arg Val Lys Gly
        115                 120
```

(2) INFORMATION FOR SEQ ID NO: 17:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 2559 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: ADN (genomic)

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION:1..2556

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 17:

```
ATG AAA GTG ATG GGG ATG CAG AGT GGT TGG ATG GGG ATG AAG AGT GGT      48
Met Lys Val Met Gly Met Gln Ser Gly Trp Met Gly Met Lys Ser Gly
        125                 130                 135
```

```
TGG TTA CTC TTC TAT CTT CTA GTA AGC TTG ATC AAG GTA ATT GGG TCT      96
Trp Leu Leu Phe Tyr Leu Leu Val Ser Leu Ile Lys Val Ile Gly Ser
    140                 145                 150

GAA CAA CAT TGG GTA ACA GTG TAC TAT GGG GTA CCA GTA TGG AGA GAA     144
Glu Gln His Trp Val Thr Val Tyr Tyr Gly Val Pro Val Trp Arg Glu
155                 160                 165                 170

GCA GAG ACA ACT CTT TTC TGT GCT TCA GAT GCT AAA GCC CAT AGT ACA     192
Ala Glu Thr Thr Leu Phe Cys Ala Ser Asp Ala Lys Ala His Ser Thr
                175                 180                 185

GAG GCT CAC AAC ATC TGG GCC ACA CAA GCA TGT GTT CCT ACT GAT CCC     240
Glu Ala His Asn Ile Trp Ala Thr Gln Ala Cys Val Pro Thr Asp Pro
            190                 195                 200

AAT CCA CAA GAA GTG CTA TTA CCC AAT GTA ACT GAA AAA TTT AAT ATG     288
Asn Pro Gln Glu Val Leu Leu Pro Asn Val Thr Glu Lys Phe Asn Met
        205                 210                 215

TGG GAA AAT AAA ATG GCA GAC CAA ATG CAA GAG GAT ATT ATC AGT CTG     336
Trp Glu Asn Lys Met Ala Asp Gln Met Gln Glu Asp Ile Ile Ser Leu
    220                 225                 230

TGG GAA CAG AGC TTA AAG CCC TGT GTT AAA TTA ACC CCA TTA TGT GTA     384
Trp Glu Gln Ser Leu Lys Pro Cys Val Lys Leu Thr Pro Leu Cys Val
235                 240                 245                 250

ACT ATG CTT TGT AAC GAT AGC TAT GGG GAG GAA AGG AAC AAT ACA AAT     432
Thr Met Leu Cys Asn Asp Ser Tyr Gly Glu Glu Arg Asn Asn Thr Asn
                255                 260                 265

ATG ACA ACA AGA GAA CCA GAC ATA GGA TAC AAA CAA ATG AAA AAT TGC     480
Met Thr Thr Arg Glu Pro Asp Ile Gly Tyr Lys Gln Met Lys Asn Cys
            270                 275                 280

TCA TTC AAT GCA ACC ACT GAG CTA ACA GAT AAA AAG AAG CAA GTT TAC     528
Ser Phe Asn Ala Thr Thr Glu Leu Thr Asp Lys Lys Lys Gln Val Tyr
        285                 290                 295

TCT CTG TTT TAT GTA GAA GAT GTA GTA CCA ATC AAT GCC TAT AAT AAA     576
Ser Leu Phe Tyr Val Glu Asp Val Val Pro Ile Asn Ala Tyr Asn Lys
    300                 305                 310

ACA TAT AGG CTA ATA AAT TGT AAT ACC ACA GCT GTG ACA CAA GCT TGT     624
Thr Tyr Arg Leu Ile Asn Cys Asn Thr Thr Ala Val Thr Gln Ala Cys
315                 320                 325                 330

CCT AAG ACT TCC TTT GAG CCA ATT CCA ATA CAT TAC TGT GCA CCA CCA     672
Pro Lys Thr Ser Phe Glu Pro Ile Pro Ile His Tyr Cys Ala Pro Pro
                335                 340                 345

GGC TTT GCC ATT ATG AAA TGT AAT GAA GGA AAC TTT AGT GGA AAT GGA     720
Gly Phe Ala Ile Met Lys Cys Asn Glu Gly Asn Phe Ser Gly Asn Gly
            350                 355                 360
```

```
AGC TGT ACA AAT GTG AGT ACT GTA CAA TGC ACA CAT GGA ATA AAG CCA     768
Ser Cys Thr Asn Val Ser Thr Val Gln Cys Thr His Gly Ile Lys Pro
        365                 370                 375

GTG ATA TCC ACT CAG TTA ATC CTA AAT GGA AGC TTA AAT ACA GAT GGA     816
Val Ile Ser Thr Gln Leu Ile Leu Asn Gly Ser Leu Asn Thr Asp Gly
    380                 385                 390

ATT GTT ATT AGA AAT GAT AGT CAC AGT AAT CTG TTG GTG CAA TGG AAT     864
Ile Val Ile Arg Asn Asp Ser His Ser Asn Leu Leu Val Gln Trp Asn
395                 400                 405                 410

GAG ACA GTG CCA ATA AAT TGT ACA AGG CCA GGA AAT AAT ACA GGA GGA     912
Glu Thr Val Pro Ile Asn Cys Thr Arg Pro Gly Asn Asn Thr Gly Gly
                415                 420                 425

CAG GTG CAG ATA GGA CCT GCT ATG ACA TTT TAT AAC ATA GAA AAA ATA     960
Gln Val Gln Ile Gly Pro Ala Met Thr Phe Tyr Asn Ile Glu Lys Ile
            430                 435                 440

GTA GGA GAC ATT AGA CAA GCA TAC TGT AAT GTC TCT AAA GAA CTA TGG    1008
Val Gly Asp Ile Arg Gln Ala Tyr Cys Asn Val Ser Lys Glu Leu Trp
        445                 450                 455

GAA CCA ATG TGG AAT AGA ACA AGA GAG GAA ATA AAG AAA ATC CTG GGG    1056
Glu Pro Met Trp Asn Arg Thr Arg Glu Glu Ile Lys Lys Ile Leu Gly
    460                 465                 470

AAA AAC AAC ATA ACC TTC AGG GCT CGA GAG AGG AAT GAA GGA GAC CTA    1104
Lys Asn Asn Ile Thr Phe Arg Ala Arg Glu Arg Asn Glu Gly Asp Leu
475                 480                 485                 490

GAA GTG ACA CAC TTA ATG TTC AAT TGT AGA GGA GAG TTT TTC TAT TGT    1152
Glu Val Thr His Leu Met Phe Asn Cys Arg Gly Glu Phe Phe Tyr Cys
                495                 500                 505

AAC ACT TCC AAA TTA TTT AAT GAG GAA TTA CTT AAC GAG ACA GGT GAG    1200
Asn Thr Ser Lys Leu Phe Asn Glu Glu Leu Leu Asn Glu Thr Gly Glu
            510                 515                 520

CCT ATT ACT CTG CCT TGT AGA ATA AGA CAG ATT GTA AAT TTG TGG ACA    1248
Pro Ile Thr Leu Pro Cys Arg Ile Arg Gln Ile Val Asn Leu Trp Thr
        525                 530                 535

AGG GTA GGA AAA GGA ATT TAT GCA CCA CCA ATT CGG GGA GTT CTT AAC    1296
Arg Val Gly Lys Gly Ile Tyr Ala Pro Pro Ile Arg Gly Val Leu Asn
    540                 545                 550

TGT ACC TCC AAT ATT ACT GGA CTG GTT CTA GAA TAT AGT GGT GGG CCT    1344
Cys Thr Ser Asn Ile Thr Gly Leu Val Leu Glu Tyr Ser Gly Gly Pro
555                 560                 565                 570

GAC ACC AAG GAA ACA ATA GTA TAT CCC TCA GGA GGA AAC ATG GTT AAT    1392
Asp Thr Lys Glu Thr Ile Val Tyr Pro Ser Gly Gly Asn Met Val Asn
```

```
                    575                 580                 585

CTC TGG AGA CAA GAG TTG TAT AAG TAC AAA GTA GTT AGC ATA GAA CCC   1440
Leu Trp Arg Gln Glu Leu Tyr Lys Tyr Lys Val Val Ser Ile Glu Pro
            590                 595                 600

ATA GGA GTA GCA CCA GGT AAA GCT AAA AGA CGC ACA GTG AGT AGA GAA   1488
Ile Gly Val Ala Pro Gly Lys Ala Lys Arg Arg Thr Val Ser Arg Glu
        605                 610                 615

AAA AGA GCA GCC TTT GGA CTA GGT GCG CTG TTT CTT GGG TTT CTT GGA   1536
Lys Arg Ala Ala Phe Gly Leu Gly Ala Leu Phe Leu Gly Phe Leu Gly
    620                 625                 630

GCA GCA GGG AGC ACT ATG GGC GCA GCG TCA ATA ACG CTG ACG GTA CAG   1584
Ala Ala Gly Ser Thr Met Gly Ala Ala Ser Ile Thr Leu Thr Val Gln
635                 640                 645                 650

GCC CGG ACA TTA TTA TCT GGG ATA GTG CAA CAG CAG AAT ATT CTG TTG   1632
Ala Arg Thr Leu Leu Ser Gly Ile Val Gln Gln Gln Asn Ile Leu Leu
                655                 660                 665

AGA GCA ATA GAG GCG CAA CAA CAT TTG TTG CAA CTC TCA ATC TGG GGC   1680
Arg Ala Ile Glu Ala Gln Gln His Leu Leu Gln Leu Ser Ile Trp Gly
            670                 675                 680

ATT AAA CAG CTC CAG GCA AAA GTC CTT GCT ATA GAA AGA TAC CTT AGG   1728
Ile Lys Gln Leu Gln Ala Lys Val Leu Ala Ile Glu Arg Tyr Leu Arg
        685                 690                 695

GAT CAG CAA ATC CTA AGT CTA TGG GGC TGC TCA GGA AAA ACA ATA TGC   1776
Asp Gln Gln Ile Leu Ser Leu Trp Gly Cys Ser Gly Lys Thr Ile Cys
    700                 705                 710

TAT ACC ACT GTG CCT TGG AAT GAG ACT TGG AGC AAC AAT ACC TCT TAT   1824
Tyr Thr Thr Val Pro Trp Asn Glu Thr Trp Ser Asn Asn Thr Ser Tyr
715                 720                 725                 730

GAT ACA ATC TGG AAT AAT TTA ACC TGG CAA CAA TGG GAT GAG AAA GTA   1872
Asp Thr Ile Trp Asn Asn Leu Thr Trp Gln Gln Trp Asp Glu Lys Val
                735                 740                 745

AGA AAC TAT TCA GGT GTC ATT TTT GGA CTT ATA GAA CAG GCA CAA GAA   1920
Arg Asn Tyr Ser Gly Val Ile Phe Gly Leu Ile Glu Gln Ala Gln Glu
            750                 755                 760

CAA CAG AAC ACA AAT GAG AAA TCA CTC TTG GAA TTG GAT CAA TGG GAC   1968
Gln Gln Asn Thr Asn Glu Lys Ser Leu Leu Glu Leu Asp Gln Trp Asp
        765                 770                 775

AGT CTG TGG AGC TGG TTT GGT ATT ACA AAA TGG CTG TGG TAT ATA AAA   2016
Ser Leu Trp Ser Trp Phe Gly Ile Thr Lys Trp Leu Trp Tyr Ile Lys
    780                 785                 790

ATA GCT ATA ATG ATA GTA GCA GGC ATT GTA GGC ATA AGA ATC ATA AGT   2064
```

```
Ile Ala Ile Met Ile Val Ala Gly Ile Val Gly Ile Arg Ile Ile Ser
795                 800                 805                 810

ATA GTA ATA ACT ATA ATA GCA AGA GTT AGG CAG GGA TAT TCT CCC CTT   2112
Ile Val Ile Thr Ile Ile Ala Arg Val Arg Gln Gly Tyr Ser Pro Leu
                815                 820                 825

TCG TTG CAG ACC CTT ATC CCA ACA GCA AGG GGA CCA GAC AGG CCA GAA   2160
Ser Leu Gln Thr Leu Ile Pro Thr Ala Arg Gly Pro Asp Arg Pro Glu
            830                 835                 840

GAA ACA GAA GGA GGC GTT GGA GAG CAA GAC AGA GGC AGA TCC GTG CGA   2208
Glu Thr Glu Gly Gly Val Gly Glu Gln Asp Arg Gly Arg Ser Val Arg
        845                 850                 855

TTA GTG AGC GGA TTC TCA GCT CTT GTC TGG GAG GAC CTC CGG AAC CTG   2256
Leu Val Ser Gly Phe Ser Ala Leu Val Trp Glu Asp Leu Arg Asn Leu
    860                 865                 870

TTG ATC TTC CTC TAC CAC CGC TTG ACA GAC TCA CTC TTG ATA CTG AGG   2304
Leu Ile Phe Leu Tyr His Arg Leu Thr Asp Ser Leu Leu Ile Leu Arg
875                 880                 885                 890

AGG ACT CTG GAA CTC CTG GGA CAG AGT CTC AGC AGG GGA CTG CAA CTA   2352
Arg Thr Leu Glu Leu Leu Gly Gln Ser Leu Ser Arg Gly Leu Gln Leu
                895                 900                 905

CTG AAT GAA CTC AGA ACA CAC TTG TGG GGA ATA CTT GCA TAT TGG GGA   2400
Leu Asn Glu Leu Arg Thr His Leu Trp Gly Ile Leu Ala Tyr Trp Gly
            910                 915                 920

AAA GAG TTA AGG GAT AGT GCT ATC AGC TTG CTT AAT ACA ACA GCT ATT   2448
Lys Glu Leu Arg Asp Ser Ala Ile Ser Leu Leu Asn Thr Thr Ala Ile
        925                 930                 935

GTA GTA GCA GAA GGA ACA GAT AGG ATT ATA GAA TTA GCA CAA AGA ATA   2496
Val Val Ala Glu Gly Thr Asp Arg Ile Ile Glu Leu Ala Gln Arg Ile
    940                 945                 950

GGA AGG GGA ATA TTA CAC ATA CCT AGA AGA ATC AGA CAA GGC CTA GAA   2544
Gly Arg Gly Ile Leu His Ile Pro Arg Arg Ile Arg Gln Gly Leu Glu
955                 960                 965                 970

AGA GCA CTG ATA TAA                                              2559
Arg Ala Leu Ile
```

(2) INFORMATION FOR SEQ ID NO: 18:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 852 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 18:

```
Met Lys Val Met Gly Met Gln Ser Gly Trp Met Gly Met Lys Ser Gly
  1               5                  10                  15

Trp Leu Leu Phe Tyr Leu Leu Val Ser Leu Ile Lys Val Ile Gly Ser
             20                  25                  30

Glu Gln His Trp Val Thr Val Tyr Tyr Gly Val Pro Val Trp Arg Glu
         35                  40                  45

Ala Glu Thr Thr Leu Phe Cys Ala Ser Asp Ala Lys Ala His Ser Thr
     50                  55                  60

Glu Ala His Asn Ile Trp Ala Thr Gln Ala Cys Val Pro Thr Asp Pro
 65                  70                  75                  80

Asn Pro Gln Glu Val Leu Leu Pro Asn Val Thr Glu Lys Phe Asn Met
                 85                  90                  95

Trp Glu Asn Lys Met Ala Asp Gln Met Gln Glu Asp Ile Ile Ser Leu
            100                 105                 110

Trp Glu Gln Ser Leu Lys Pro Cys Val Lys Leu Thr Pro Leu Cys Val
        115                 120                 125

Thr Met Leu Cys Asn Asp Ser Tyr Gly Glu Glu Arg Asn Asn Thr Asn
    130                 135                 140

Met Thr Thr Arg Glu Pro Asp Ile Gly Tyr Lys Gln Met Lys Asn Cys
145                 150                 155                 160

Ser Phe Asn Ala Thr Thr Glu Leu Thr Asp Lys Lys Lys Gln Val Tyr
                165                 170                 175

Ser Leu Phe Tyr Val Glu Asp Val Val Pro Ile Asn Ala Tyr Asn Lys
            180                 185                 190

Thr Tyr Arg Leu Ile Asn Cys Asn Thr Thr Ala Val Thr Gln Ala Cys
        195                 200                 205

Pro Lys Thr Ser Phe Glu Pro Ile Pro Ile His Tyr Cys Ala Pro Pro
    210                 215                 220

Gly Phe Ala Ile Met Lys Cys Asn Glu Gly Asn Phe Ser Gly Asn Gly
225                 230                 235                 240

Ser Cys Thr Asn Val Ser Thr Val Gln Cys Thr His Gly Ile Lys Pro
                245                 250                 255

Val Ile Ser Thr Gln Leu Ile Leu Asn Gly Ser Leu Asn Thr Asp Gly
            260                 265                 270

Ile Val Ile Arg Asn Asp Ser His Ser Asn Leu Leu Val Gln Trp Asn
```

```
        275                 280                 285

Glu Thr Val Pro Ile Asn Cys Thr Arg Pro Gly Asn Asn Thr Gly Gly
    290                 295                 300

Gln Val Gln Ile Gly Pro Ala Met Thr Phe Tyr Asn Ile Glu Lys Ile
305                 310                 315                 320

Val Gly Asp Ile Arg Gln Ala Tyr Cys Asn Val Ser Lys Glu Leu Trp
                325                 330                 335

Glu Pro Met Trp Asn Arg Thr Arg Glu Glu Ile Lys Lys Ile Leu Gly
            340                 345                 350

Lys Asn Asn Ile Thr Phe Arg Ala Arg Glu Arg Asn Glu Gly Asp Leu
        355                 360                 365

Glu Val Thr His Leu Met Phe Asn Cys Arg Gly Glu Phe Phe Tyr Cys
    370                 375                 380

Asn Thr Ser Lys Leu Phe Asn Glu Glu Leu Leu Asn Glu Thr Gly Glu
385                 390                 395                 400

Pro Ile Thr Leu Pro Cys Arg Ile Arg Gln Ile Val Asn Leu Trp Thr
                405                 410                 415

Arg Val Gly Lys Gly Ile Tyr Ala Pro Pro Ile Arg Gly Val Leu Asn
            420                 425                 430

Cys Thr Ser Asn Ile Thr Gly Leu Val Leu Glu Tyr Ser Gly Gly Pro
        435                 440                 445

Asp Thr Lys Glu Thr Ile Val Tyr Pro Ser Gly Gly Asn Met Val Asn
    450                 455                 460

Leu Trp Arg Gln Glu Leu Tyr Lys Tyr Lys Val Val Ser Ile Glu Pro
465                 470                 475                 480

Ile Gly Val Ala Pro Gly Lys Ala Lys Arg Arg Thr Val Ser Arg Glu
                485                 490                 495

Lys Arg Ala Ala Phe Gly Leu Gly Ala Leu Phe Leu Gly Phe Leu Gly
            500                 505                 510

Ala Ala Gly Ser Thr Met Gly Ala Ala Ser Ile Thr Leu Thr Val Gln
        515                 520                 525

Ala Arg Thr Leu Leu Ser Gly Ile Val Gln Gln Gln Asn Ile Leu Leu
    530                 535                 540

Arg Ala Ile Glu Ala Gln Gln His Leu Leu Gln Leu Ser Ile Trp Gly
545                 550                 555                 560

Ile Lys Gln Leu Gln Ala Lys Val Leu Ala Ile Glu Arg Tyr Leu Arg
                565                 570                 575
```

```
Asp Gln Gln Ile Leu Ser Leu Trp Gly Cys Ser Gly Lys Thr Ile Cys
            580                 585                 590

Tyr Thr Thr Val Pro Trp Asn Glu Thr Trp Ser Asn Asn Thr Ser Tyr
        595                 600                 605

Asp Thr Ile Trp Asn Asn Leu Thr Trp Gln Gln Trp Asp Glu Lys Val
    610                 615                 620

Arg Asn Tyr Ser Gly Val Ile Phe Gly Leu Ile Glu Gln Ala Gln Glu
625                 630                 635                 640

Gln Gln Asn Thr Asn Glu Lys Ser Leu Leu Glu Leu Asp Gln Trp Asp
                645                 650                 655

Ser Leu Trp Ser Trp Phe Gly Ile Thr Lys Trp Leu Trp Tyr Ile Lys
            660                 665                 670

Ile Ala Ile Met Ile Val Ala Gly Ile Val Gly Ile Arg Ile Ile Ser
        675                 680                 685

Ile Val Ile Thr Ile Ile Ala Arg Val Arg Gln Gly Tyr Ser Pro Leu
    690                 695                 700

Ser Leu Gln Thr Leu Ile Pro Thr Ala Arg Gly Pro Asp Arg Pro Glu
705                 710                 715                 720

Glu Thr Glu Gly Gly Val Gly Glu Gln Asp Arg Gly Arg Ser Val Arg
                725                 730                 735

Leu Val Ser Gly Phe Ser Ala Leu Val Trp Glu Asp Leu Arg Asn Leu
            740                 745                 750

Leu Ile Phe Leu Tyr His Arg Leu Thr Asp Ser Leu Leu Ile Leu Arg
        755                 760                 765

Arg Thr Leu Glu Leu Leu Gly Gln Ser Leu Ser Arg Gly Leu Gln Leu
    770                 775                 780

Leu Asn Glu Leu Arg Thr His Leu Trp Gly Ile Leu Ala Tyr Trp Gly
785                 790                 795                 800

Lys Glu Leu Arg Asp Ser Ala Ile Ser Leu Leu Asn Thr Thr Ala Ile
                805                 810                 815

Val Val Ala Glu Gly Thr Asp Arg Ile Ile Glu Leu Ala Gln Arg Ile
            820                 825                 830

Gly Arg Gly Ile Leu His Ile Pro Arg Arg Ile Arg Gln Gly Leu Glu
        835                 840                 845

Arg Ala Leu Ile
    850
```

(2) INFORMATION FOR SEQ ID NO: 19:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 639 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: ADN (genomic)

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION:1..636

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 19:

```
ATG GGA AAG ATT TGG TCA AAG AGC AGC CTA GTA GGA TGG CCA GAA ATC     48
Met Gly Lys Ile Trp Ser Lys Ser Ser Leu Val Gly Trp Pro Glu Ile
        855                 860                 865

AGA GAA AGA ATG AGA AGA CAA ACG CAA GAA CCA GCA GTA GAG CCA GCA     96
Arg Glu Arg Met Arg Arg Gln Thr Gln Glu Pro Ala Val Glu Pro Ala
    870                 875                 880

GTA GGA GCA GGA GCA GCT TCT CAA GAT CTA GCT AAT CGA GGG GCC ATC    144
Val Gly Ala Gly Ala Ala Ser Gln Asp Leu Ala Asn Arg Gly Ala Ile
885                 890                 895                 900

ACC ATA AGA AAT ACT AGA GAC AAT AAT GAA AGT ATA GCT TGG CTA GAA    192
Thr Ile Arg Asn Thr Arg Asp Asn Asn Glu Ser Ile Ala Trp Leu Glu
                905                 910                 915

GCA CAA GAA GAA GAA GAG GAA GTA GGC TTT CCA GTA CGC CCT CAG GTA    240
Ala Gln Glu Glu Glu Glu Glu Val Gly Phe Pro Val Arg Pro Gln Val
            920                 925                 930

CCA TTA AGG CCA ATA ACC TAT AAA CAG GCT TTT GAT CTT TCC TTC TTT    288
Pro Leu Arg Pro Ile Thr Tyr Lys Gln Ala Phe Asp Leu Ser Phe Phe
        935                 940                 945

TTA AAA GAT AAG GGG GGA CTG GAA GGG CTA GTT TGG TCC AGA AAA AGG    336
Leu Lys Asp Lys Gly Gly Leu Glu Gly Leu Val Trp Ser Arg Lys Arg
    950                 955                 960

CAA GAT ATT CTA GAC CTC TGG ATG TAT CAC ACA CAA GGC ATC CTC CCT    384
Gln Asp Ile Leu Asp Leu Trp Met Tyr His Thr Gln Gly Ile Leu Pro
965                 970                 975                 980

GAC TGG CAT AAC TAC ACA CCA GGG CCA GGA ATT AGA TAC CCC GTA ACC    432
Asp Trp His Asn Tyr Thr Pro Gly Pro Gly Ile Arg Tyr Pro Val Thr
                985                 990                 995

TTT GGA TGG TGC TTC AAA CTA GTA CCA TTG TCA GCT GAA GAA GTA GAA    480
```

```
Phe Gly Trp Cys Phe Lys Leu Val Pro Leu Ser Ala Glu Glu Val Glu
            1000                1005                1010

GAG GCT AAT GAA GGA GAC AAC AAT GCC CTC TTA CAC CCC ATA TGT CAA    528
Glu Ala Asn Glu Gly Asp Asn Asn Ala Leu Leu His Pro Ile Cys Gln
        1015                1020                1025

CAT GGA GCA GAT GAT GAT CAT AAA GAA GTG TTG GTG TGG CGA TTT GAC    576
His Gly Ala Asp Asp Asp His Lys Glu Val Leu Val Trp Arg Phe Asp
    1030                1035                1040

AGC TCC CTA GCA AGA AGA CAT GTA GCA AGA GAG CTG CAT CCG GAG TTT    624
Ser Ser Leu Ala Arg Arg His Val Ala Arg Glu Leu His Pro Glu Phe
1045                1050                1055                1060

TAC AAG AAC TGC TGA                                            639
Tyr Lys Asn Cys
```

(2) INFORMATION FOR SEQ ID NO: 20:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 212 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 20:

```
Met Gly Lys Ile Trp Ser Lys Ser Ser Leu Val Gly Trp Pro Glu Ile
  1               5                  10                  15

Arg Glu Arg Met Arg Arg Gln Thr Gln Glu Pro Ala Val Glu Pro Ala
             20                  25                  30

Val Gly Ala Gly Ala Ala Ser Gln Asp Leu Ala Asn Arg Gly Ala Ile
         35                  40                  45

Thr Ile Arg Asn Thr Arg Asp Asn Asn Glu Ser Ile Ala Trp Leu Glu
     50                  55                  60

Ala Gln Glu Glu Glu Glu Glu Val Gly Phe Pro Val Arg Pro Gln Val
 65                  70                  75                  80

Pro Leu Arg Pro Ile Thr Tyr Lys Gln Ala Phe Asp Leu Ser Phe Phe
                 85                  90                  95

Leu Lys Asp Lys Gly Gly Leu Glu Gly Leu Val Trp Ser Arg Lys Arg
             100                 105                 110

Gln Asp Ile Leu Asp Leu Trp Met Tyr His Thr Gln Gly Ile Leu Pro
         115                 120                 125

Asp Trp His Asn Tyr Thr Pro Gly Pro Gly Ile Arg Tyr Pro Val Thr
```

130 135 140

Phe Gly Trp Cys Phe Lys Leu Val Pro Leu Ser Ala Glu Glu Val Glu
145 150 155 160

Glu Ala Asn Glu Gly Asp Asn Asn Ala Leu Leu His Pro Ile Cys Gln
165 170 175

His Gly Ala Asp Asp Asp His Lys Glu Val Leu Val Trp Arg Phe Asp
180 185 190

Ser Ser Leu Ala Arg Arg His Val Ala Arg Glu Leu His Pro Glu Phe
195 200 205

Tyr Lys Asn Cys
210

(2) INFORMATION FOR SEQ ID NO: 21:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = «PRIMER»

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 21:

ATTGCGTACT CACACTTCCG 20

(2) INFORMATION FOR SEQ ID NO: 22:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 17 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = «PRIMER»

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 22:

GGCAAGCAGG GAGCTGG 17

(2) INFORMATION FOR SEQ ID NO: 23:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: simple

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = «PRIMER»

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 23:

TCCTTGAGCA GTCTGGAC 18

(2) INFORMATION FOR SEQ ID NO: 24:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = «PRIMER»

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 24:

GAACAGGAGG ATTAGCAG 18

(2) INFORMATION FOR SEQ ID NO: 25:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = «PRIMER»

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 25:

AGCAGAGGCT ATGTCACA 18

(2) INFORMATION FOR SEQ ID NO: 26:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 19 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = «PRIMER»

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 26:

TGTAAGGCCC CTAGAAGAG 19

(2) INFORMATION FOR SEQ ID NO: 27:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = «PRIMER»

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 27:

ACAGAGAACT CTCTGTAC 18

(2) INFORMATION FOR SEQ ID NO: 28:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = «PRIMER»

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 28:

AAGAAAAGCA GTTGGTAC 18

(2) INFORMATION FOR SEQ ID NO: 29:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 17 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = «PRIMER»

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 29:

TTTCTTCCCT GTATGTC 17

(2) INFORMATION FOR SEQ ID NO: 30:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 18 base pairs
(B) TYPE: nucleic acid

(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = «PRIMER»

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 30:

GTTATATGGA TTCTCAGG 18

(2) INFORMATION FOR SEQ ID NO: 31:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 19 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = «PRIMER»

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 31:

TGGCAGCACA TTATACTGG 19

(2) INFORMATION FOR SEQ ID NO: 32:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 23 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = «PRIMER»

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 32:

ATCATTTACC AGTACATGGA CGA 23

(2) INFORMATION FOR SEQ ID NO: 33:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = «PRIMER»

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 33:

TGTCAGGGGT CGTAAAGC 18

(2) INFORMATION FOR SEQ ID NO: 34:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = «PRIMER»

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 34:

TCCTCTGGAT GGGATATG 18

(2) INFORMATION FOR SEQ ID NO: 35:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = «PRIMER»

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 35:

TCTATCCAGG AATCAGAG 18

(2) INFORMATION FOR SEQ ID NO: 36:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = «PRIMER»

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 36:

AATGAGATCT GCCCATAC 18

(2) INFORMATION FOR SEQ ID NO: 37:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: simple

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = «PRIMER»

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 37:

TGACAGATAG GGGAAGAC 18

(2) INFORMATION FOR SEQ ID NO: 38:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = «PRIMER»

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 38:

AACCGCCATT TGCACTGC 18

(2) INFORMATION FOR SEQ ID NO: 39:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = «PRIMER»

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 39:

ACATGGACCG CCACAAGG 18

(2) INFORMATION FOR SEQ ID NO: 40:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = «PRIMER»

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 40:

AGCAACAGAC ATACAGAC 18

(2) INFORMATION FOR SEQ ID NO: 41:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = «PRIMER»

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 41:

AAAGTAGTCC CACGTAGG 18

(2) INFORMATION FOR SEQ ID NO: 42:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = «PRIMER»

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 42:

ATATCCCAGT AGGTCAGG 18

(2) INFORMATION FOR SEQ ID NO: 43:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = «PRIMER»

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 43:

TCTAGCACTA ACAGCCTG 18

(2) INFORMATION FOR SEQ ID NO: 44:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = «PRIMER»

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 44:

ACTCTTACTG CTCTGAGG 18

(2) INFORMATION FOR SEQ ID NO: 45:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = «PRIMER»

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 45:

CCATAGTACA CTGTTACC 18

(2) INFORMATION FOR SEQ ID NO: 46:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = «PRIMER»

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 46:

CATAGCTATC GTTACAAAGC 20

(2) INFORMATION FOR SEQ ID NO: 47:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = «PRIMER»

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 47:

TCATAATGGC AAAGCCTG 18

(2) INFORMATION FOR SEQ ID NO: 48:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = «PRIMER»

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 48:

CTATTCCACA TTGGTTCC 18

(2) INFORMATION FOR SEQ ID NO: 49:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = «PRIMER»

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 49:

ATTCTAGAAC CAGTCCAG 18

(2) INFORMATION FOR SEQ ID NO: 50:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = «PRIMER»

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 50:

CCTTAGGGAT CAGCAAATCC 20

(2) INFORMATION FOR SEQ ID NO: 51:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 18 base pairs
(B) TYPE: nucleic acid

(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = «PRIMER»

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 51:

TGGGACAGTC TGTGGAGC 18

(2) INFORMATION FOR SEQ ID NO: 52:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = «PRIMER»

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 52:

TTCTCAGCTC TTGTCTGG 18

(2) INFORMATION FOR SEQ ID NO: 53:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = «PRIMER»

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 53:

ATTAAGCAAG CTGATAGC 18

(2) INFORMATION FOR SEQ ID NO: 54:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 16 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = «PRIMER»

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 54:

GTGCTTCTA GCCAAG 16

(2) INFORMATION FOR SEQ ID NO: 55:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = «PRIMER»

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 55:

GCTCCATGTT GACATATG 18

(2) INFORMATION FOR SEQ ID NO: 56:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = «PRIMER»

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 56:

AGAGAGACCC AGTACAAG 18

(2) INFORMATION FOR SEQ ID NO: 57:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = "PRIMER"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 57:

ATAAAAGCAG CCGCTTCTCG 20

(2) INFORMATION FOR SEQ ID NO: 58:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 35 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 58:

Cys Thr Arg Pro Gly Asn Asn Thr Gly Gly Gln Val Gln Ile Gly Pro
1 5 10 15

Ala Met Thr Phe Tyr Asn Ile Glu Lys Ile Val Gly Asp Ile Arg Gln
20 25 30

Ala Tyr Cys
35

(2) INFORMATION FOR SEQ ID NO: 59:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 35 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 59:

Cys His Arg Pro Gly Asn Asn Thr Arg Gly Glu Val Gln Ile Gly Pro
1 5 10 15

Gly Met Thr Phe Tyr Asn Ile Glu Asn Val Tyr Gly Asp Thr Arg Ser
20 25 30

Ala Tyr Cys
35

(2) INFORMATION FOR SEQ ID NO: 60:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 35 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 60:

Cys Ile Arg Pro Gly Asn Arg Thr Tyr Arg Asn Leu Gln Ile Gly Pro
1 5 10 15

Gly Met Thr Phe Tyr Asn Val Glu Ile Ala Thr Gly Asp Ile Arg Lys
20 25 30

Ala Phe Cys
35

(2) INFORMATION FOR SEQ ID NO: 61:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGHT: 35 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: simple
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 61:

Cys Thr Arg Pro Asn Asn Asn Thr Arg Lys Ser Val Arg Ile Gly Pro
1 5 10 15

Gly Gln Ala Phe Tyr Ala Thr Gly Asp Ile Ile Gly Asp Ile Arg Gln
20 25 30

Ala His Cys
35

MICROORGANISMS

Optional Sheet in connection with the microorganism referred to on page 3, line 30 of the description

A. IDENTIFICATION OF DEPOSIT

Further deposits are identified on an additional sheet ☐

Name of depositary institution

Collection Nationale de Cultures de Micro-organismes

Address of depositary institution (including postal code and country)

28 rue du Docteur Roux, 75724 PARIS CEDEX 15

Date of deposit	Accession Number
July 2, 1996	I-1753

B. ADDITIONAL INDICATIONS (leave blank if not applicable). This information is continued on a separate attached sheet ☐

"With regard to the nominations in which a European patent is applied for, until the publication of the mention of the grant of the European patent or until the date on which the application shall be refused or withdrawn or shall be deemed to be withdrawn, a sample of the deposited microorganism shall be available only by the issue of a sample to an expert nominated by the requester. (Rule 28.4) of the EPC)".

C. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)

ALL PCT CONTRACTING STATES

D. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)

The indications listed below will be submitted to the International Bureau later (Specify the general nature of the indications e.g., "Accession Number of Deposit")

E. ☐ This sheet was received with the international application when filed (to be checked by the receiving Office)

(illegible signature)

(Authorized Officer)

☐ The date of receipt (from the applicant) by the International Bureau was

(Authorized Officer)

AUSTRALIAN PATENT OFFICE

(January 1985)

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. An isolated non-M, non-O strain of HIV-1, a sample of which was deposited on 2 July 1996 under number I-1753 (designated YBF30) in the Collection Nationale de Cultures de Microorganismes (National Collection of Microorganism Cultures)kept by the Pasteur Institute.

2. An isolated nucleic acid sequence, wherein the sequence is derived from the strain according to Claim 1 and is selected from the group consisting of: SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19 and SEQ ID NOS:21 to 57, and wherein said sequence is capable of hybridizing with a nucleic acid sequence which is derived from a non-M, non-O HIV-1 virus.

3. An isolated oligonucleotide wherein said oligonucleotide comprises a nucleic acid sequence selected from the group consisting of SEQ ID NOS:21 to 57, and wherein said oligonucleotide is capable of being used as a primer or as a probe for detecting a non-M, non-O HIV-1 strain according to Claim 1.

4. An isolated non-M, non-O strain HIV-1 virus, wherein the virus exhibits the following characteristics:

(a) little or no serological reactivity with regard to proteins of the M and O groups and strong serological reactivity with regard to proteins which are derived from the YBF30 strain according to Claim 1 or the CPZGAB SIV strain;

(b) absence of genomic amplification when using

primers form the *env* and *gag* regions of the HIV-1 viruses of the M and O groups;

(c) genomic amplification in the presence of the primers which are derived from the YBF30 strain according to Claim 3; and

(d) greater than 70% sequence homology with the polynucleotide or polypeptide products of the envelope gene with regard to the corresponding polypeptide or polynucleotide products of the envelope gene of YBF30 strain.

5. An oligonucleotide which comprises a nucleic acid sequence selected from the group consisting of: SEQ ID NOS: 21 to 57, and wherein said oligonucleotide is capable of being used as a primer or as a probe for detecting a non-M, non-O strain of HIV-1 according to Claim 4.

6. A method of *in vitro* diagnosis of non-M, non-O strain HIV-1 virus comprising the steps of:

(a) providing a biological sample suspected of comprising a nucleic acid sequence to be detected;

(b) hybridizing the nucleic acid of (a) with at least one nucleic acid sequence according to Claim 2 or Claim 3; and

(c) detecting the presence of the hybridized nucleic acid sequence.

7. An isolated peptide capable of being expressed by a non-M, non-O strain of HIV-1 virus according to Claim 1 or Claim 4 or encoded by a nucleotide sequence according to Claim 2, wherein said peptide is capable of:

(a) being recognized by antibodies which are induced by a non-M, non-O HIV-1 virus according to Claim 1 or Claim 4, or a variant of this virus, and which are

present in a biological sample which is obtained following an infection with a non-M, non-O HIV-1 strain; and/or

(b) inducing the production of anti-non-M, non-O HIV-1 antibodies.

8. A peptide according to Claim 7, wherein said peptide is expressed by a nucleic acid sequence selected from the group consisting of: SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:58 and SEQ ID NO:20.

9. An immunogenic composition comprising one or more translation products of the nucleotide sequences according to Claim 2 and/or one of the peptides according to Claim 7 or Claim 8.

10. An isolated antibody directed against one or more of the peptides according to Claim 7 or Claim 8.

11. A method for the *in vitro* diagnosis of a non-M, non-O strain of HIV-1 virus, comprising the steps of:

(a) providing a biological sample to be tested;

(b) combining the sample of (a) with an antibody according to Claim 10 [which may possibly be combined with anti-CPZGAB SIV antibodies]; and

(c) detecting the presence of antibody-antigen complexes.

12. A method according to Claim 11, wherein the antibody of step (b) is also combined with anti-CPZGAB SIV antibodies.

13. A reagent for diagnosing a non-M, non-O strain

HIV-1 virus, comprising a nucleic acid or peptide sequence according to any one of Claims 2, 3, 7 or 8.

14. A method for screening and typing a non-M, non-O strain HIV-1 virus, comprising the steps of:

(a) bringing a nucleic acid sequence selected from the group consisting of SEQ ID NOS: 2, 3, 5, 7, 9, 11, 13, 15, 17, 19 and 21 to 57 into contact with the nucleic acid of the virus to be typed; and

(b) detecting the hybrid which is formed.

15. A kit for diagnosing a non-M, non-O strain HIV-1 virus, comprising a reagent according to Claim 13.

16. An isolated virus according to claim 1, substantially as herein described with reference to any one of the examples or figures.

17. An isolated virus according to claim 4, substantially as herein described with reference to any one of the examples or figures.

Dated this 16th day of July 2001

INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) and ASSISTANCE PUBLIQUE-HOPITAUX DE PARIS and INSTITUT PASTEUR

By their Patent Attorneys

GRIFFITH HACK

Fellows Institute of Patent and Trade Mark Attorneys of Australia

YLG	*ltr*	A T T G C G T A C T C A C A C T T C C G
LPBS.1	*ltr*	G G C A A G C A G G G A G C T G G
GAG Y AS1.1	*ltr*	T C C T T G A G C A G T C T G G A C
GAG Y AS1	*gag*	G A A C A G G A G G A T T A G C A G
Gag 6	*gag*	A G C A G A G G C T A T G T C A C A
GAG Y S1	*gag*	T G T A A G G C C C C T A G A A G A G
GAG Y S1.1	*gag*	A C A G A G A A A C T C T C T G T A C
GAG Y S1.2	*gag*	A A G A A A A G C A G T T G G T A-C
YRT AS 1.3	*pol*	T T T C T T C C C T G T A T G T C
YRT AS1.2	*pol*	G T T A T A T G G A T T C T C A G G
YRT AS1.1	*pol*	T G G C A G C A C A T T A T A C T G G
YRT2	*pol*	A T C A T T T A C C A G T A C A T G G A C G A
YRT AS1	*pol*	T G T C A G G G G T C G T A A A G C
YRT2-1	*pol*	T C C T C T G G A T G G G A T A T G
YRT2-2	*pol*	T C T A T C C A G G A A T C A G A G
YRT-3	*pol*	A A T G A G A T C T G C C C A T A C
YRT2-4	*pol*	T G A C A G A T A G G G G A A G A C
4481-1	*pol*	A A C C G C C A T T T G C A C T G C
4481-2	*pol*	A C A T G G A C C G C C A C A A G G
4235.1	*pol*	A G C A A C A G A C A T A C A G A C
4235.2	*vif*	A A A G T A G T C C C A C G T A G G
4235.3	*tat*	A T A T C C C A G T A G G T C A G G
4235.4	*tat*	T C T A G C A C T A A C A G C C T G
SK69.6	*env*	A C T C T T A C T G C T C T G A G G
SK69.5	*env*	C C A T A G T A C A C T G T T A C C
SK69.4	*env*	C A T A G C T A T C G T T A C A A A G C
SK69.3	*env*	T C A T A A A T G G C A A A G C C T G
SK69.2	*env*	C T A T T C C A C A T T G G T T C C
SK69.1	*env*	A T T C T A G A A C C A G T C C A G
SK68.1	*env*	C C T T A G G G A T C A G C A A A T C C .
SK68.2	*env*	T G G G A C A G T C T G T G G A G C
SK68.3	*env*	T T C T C A G C T C T T G T C T G G
LSI AS1.3	*nef*	A T T A A G C A A G C T G A T A G C
LSIAS1.2	*nef*	T G T G C T T C T A G C C A A G
LSI AS 1.1	*ltr*	G C T C C A T G T T G A C A T A T G
LSi A1	*ltr*	A G A G A G A C C C A G T A C A A G
YLPA	*ltr*	A T A A A A G C A G C C G C T T C T C G

FIGURE 1

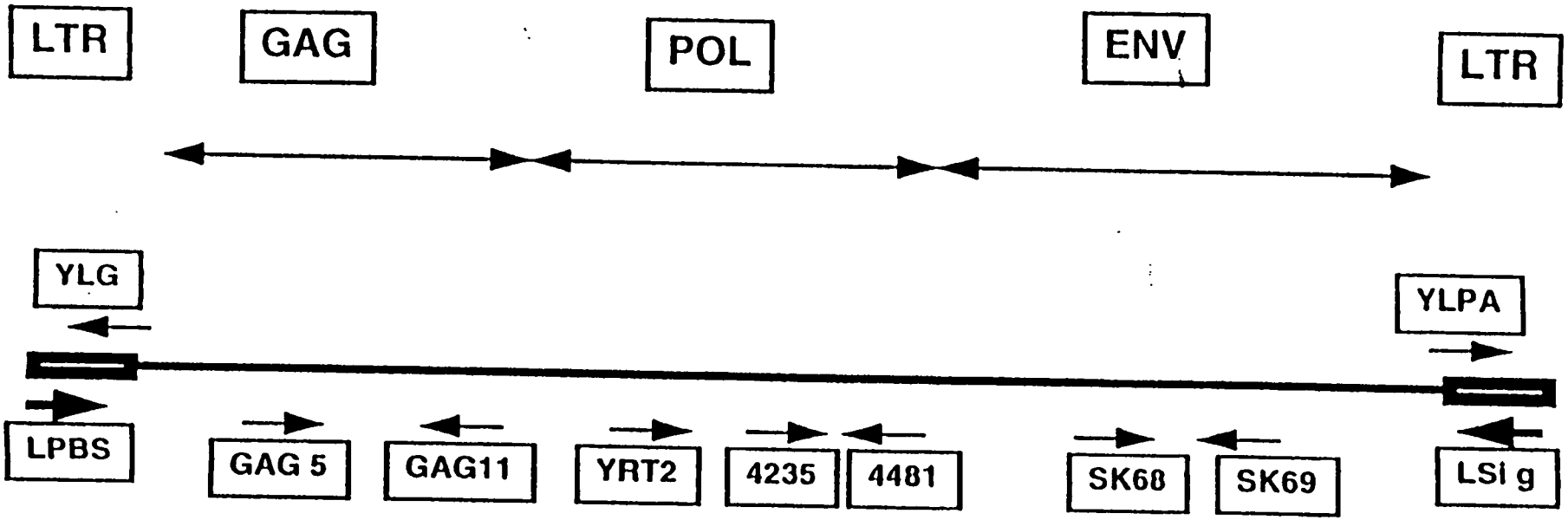

LTR
GAG
POL
ENV
LTR
YLG
YLPA
LPBS
GAG 5
GAG11
YRT2
4235
4481
SK68
SK69
LSI g

FIGURE 2

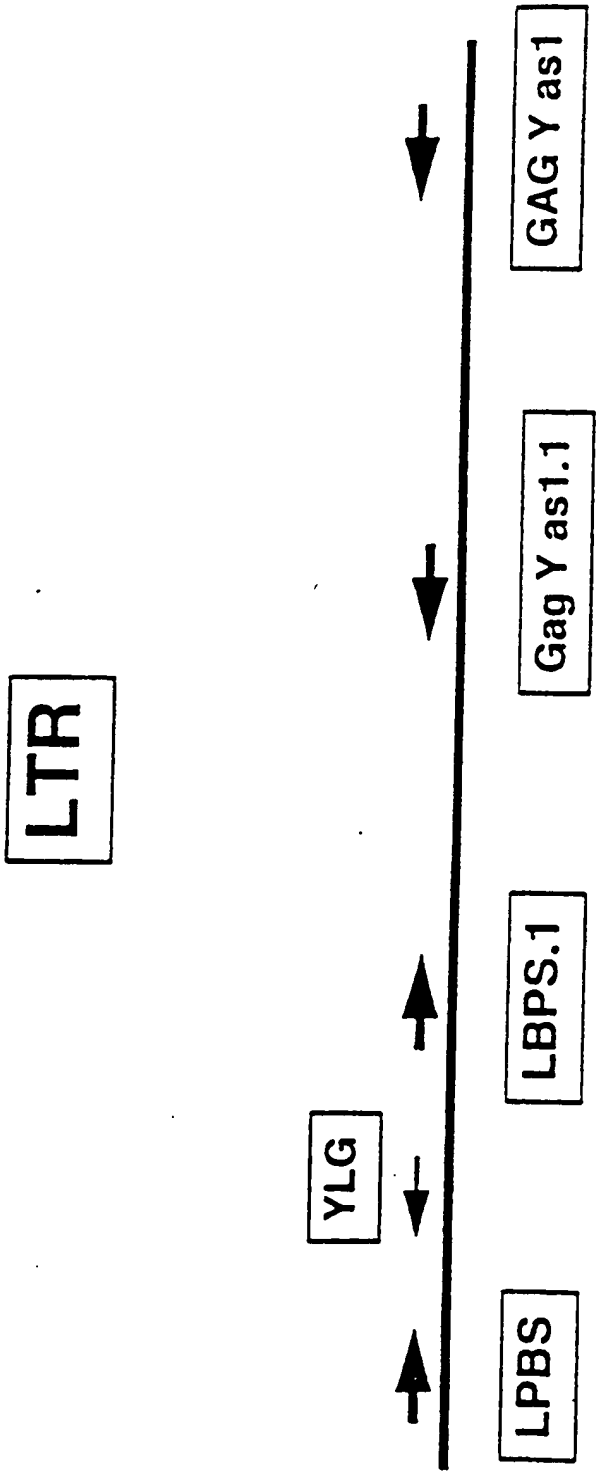


FIGURE 3

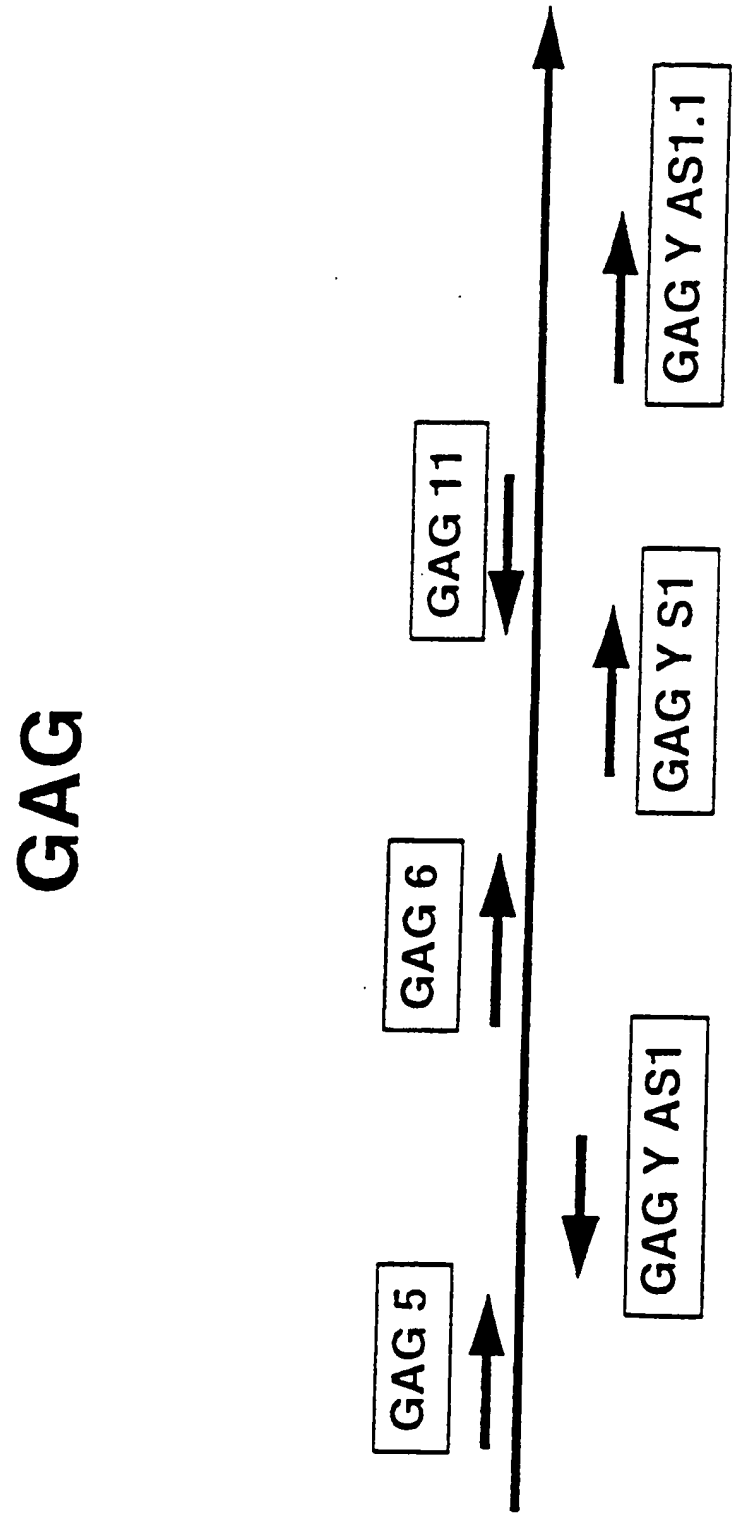


FIGURE 4

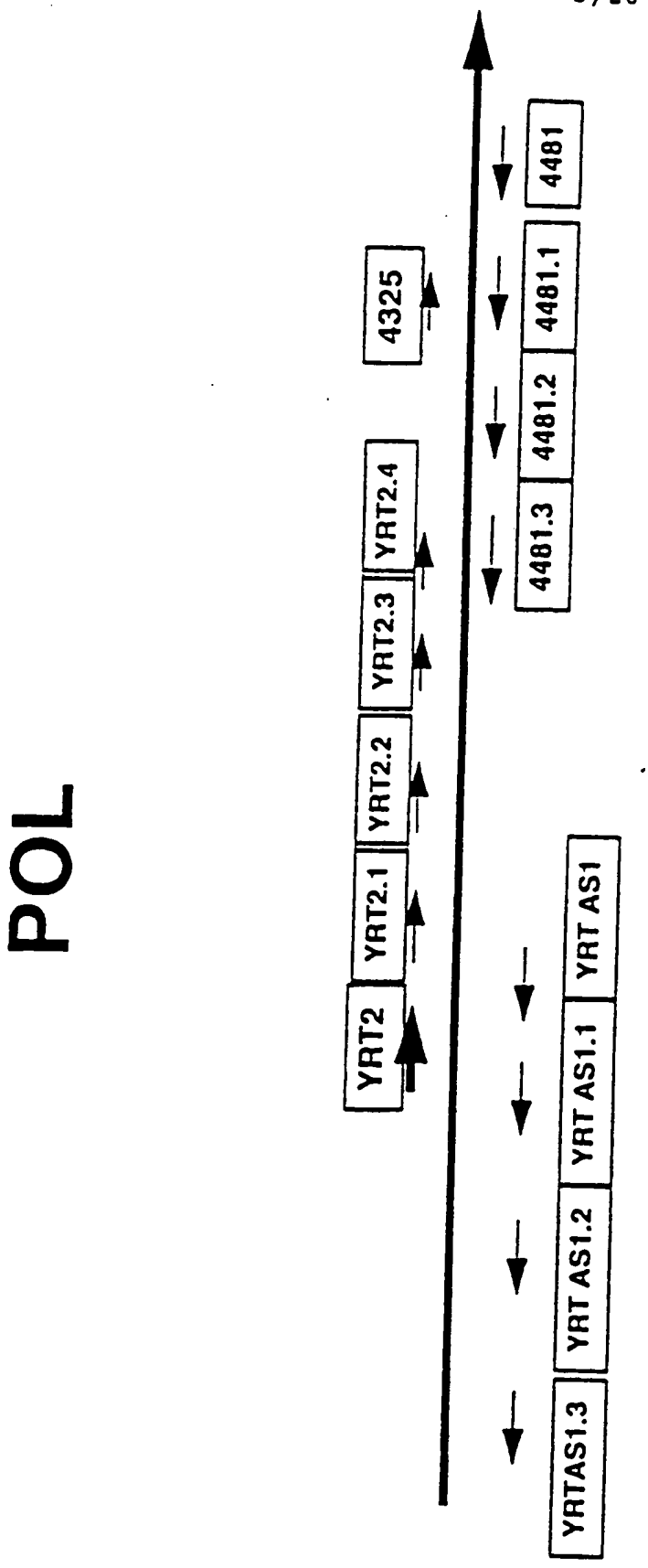

POL
YRT2
YRT2.1
YRT2.2
YRT2.3
YRT2.4
4325
4481.3
4481.2
4481.1
4481
YRTAS1.3
YRT AS1.2
YRT AS1.1
YRT AS1

FIGURE 5

ENV

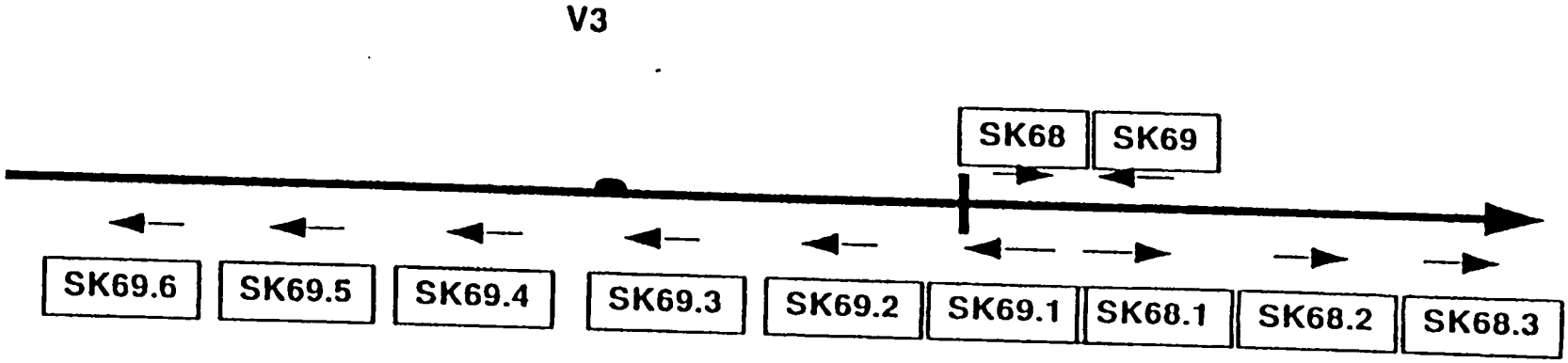

V3
SK68
SK69
SK69.6
SK69.5
SK69.4
SK69.3
SK69.2
SK69.1
SK68.1
SK68.2
SK68.3

FIGURE 6

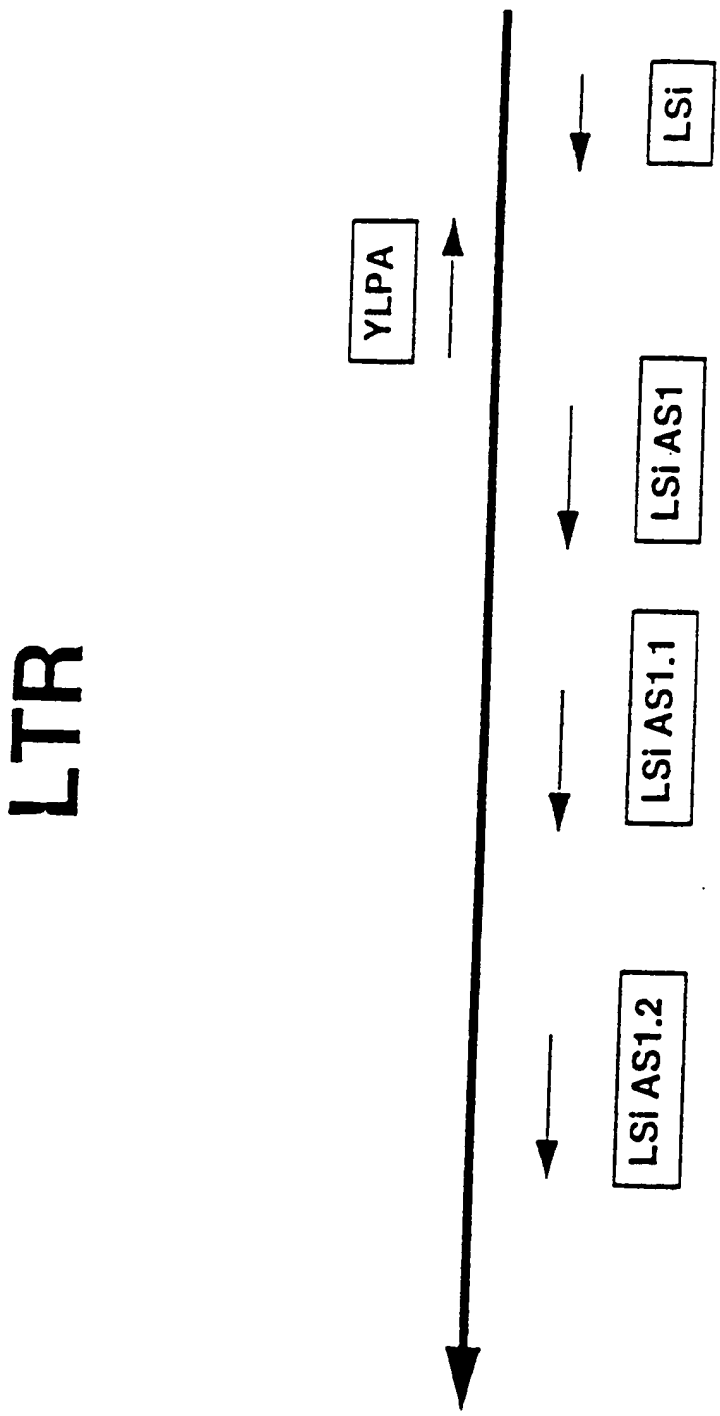


FIGURE 7

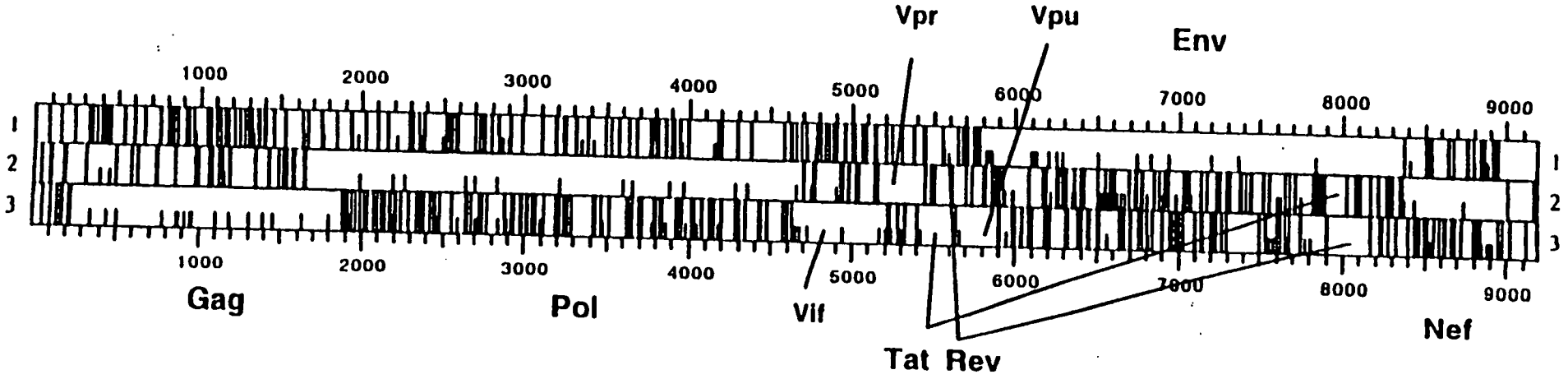

Vpr
Vpu
Env
1000
2000
3000
4000
5000
6000
7000
8000
9000
1
2
3
Gag
Pol
Vif
Tat
Rev
Nef

FIGURE 8

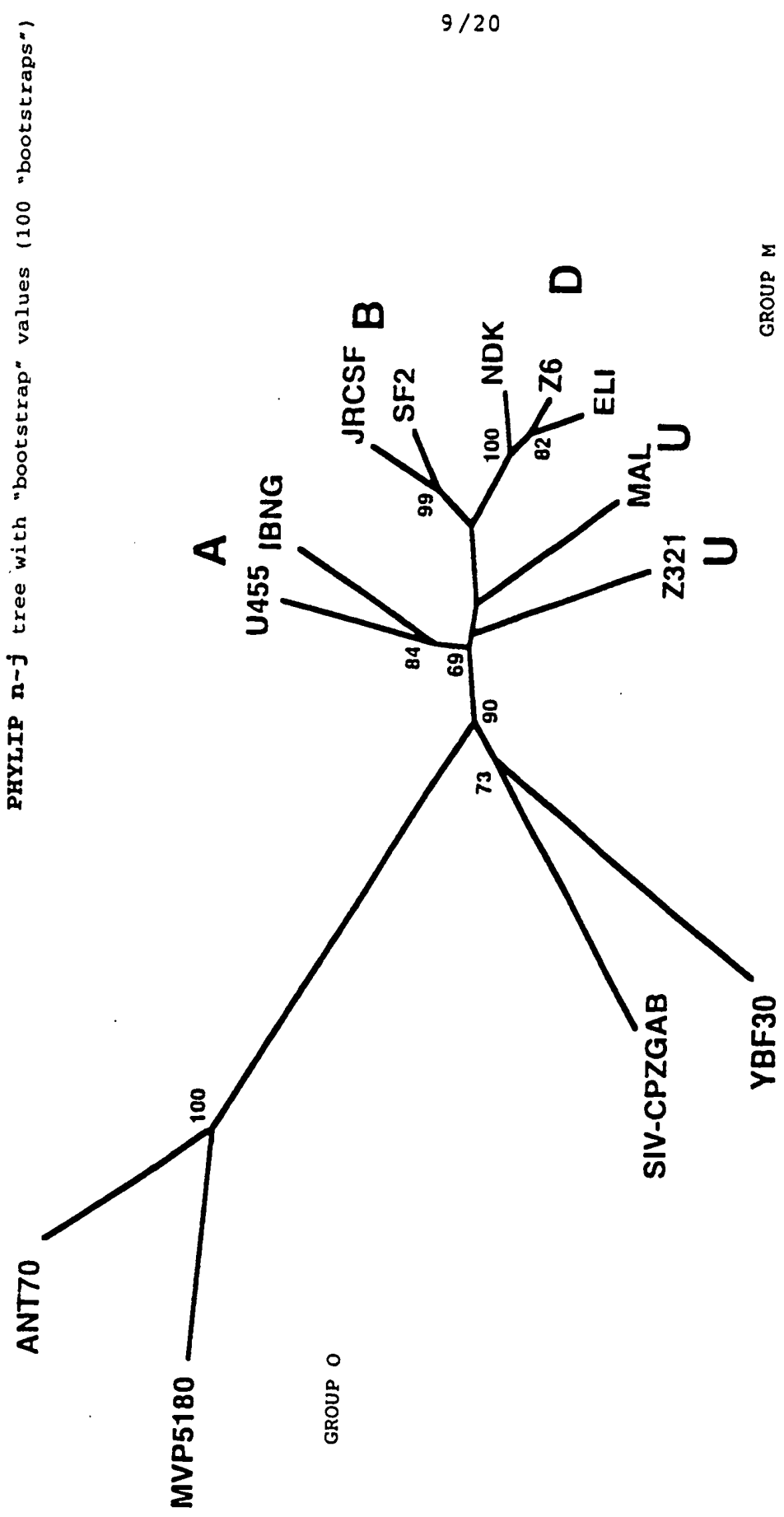
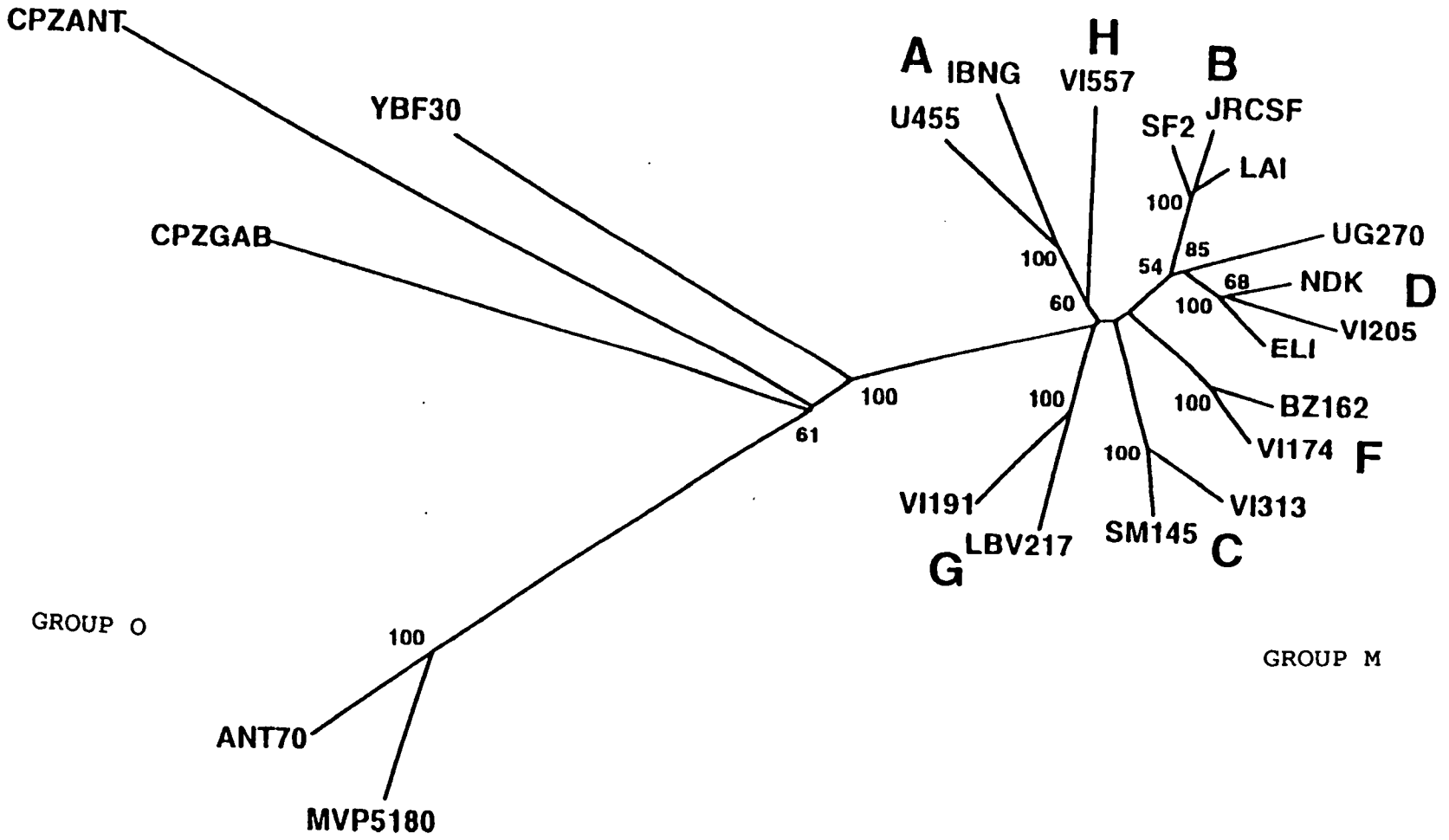

YBF30 LTR
464 nt after "bootstrapping"
PHYLIP n-j tree with "bootstrap" values (100 "bootstraps")
ANT70
MVP5180
100
GROUP O
A
U455
IBNG
B
JRCSF
SF2
99
NDK
100
Z6
82
ELI
D
MAL
U
Z321
U
84
69
90
73
SIV-CPZGAB
YBF30
GROUP M

FIGURE 9

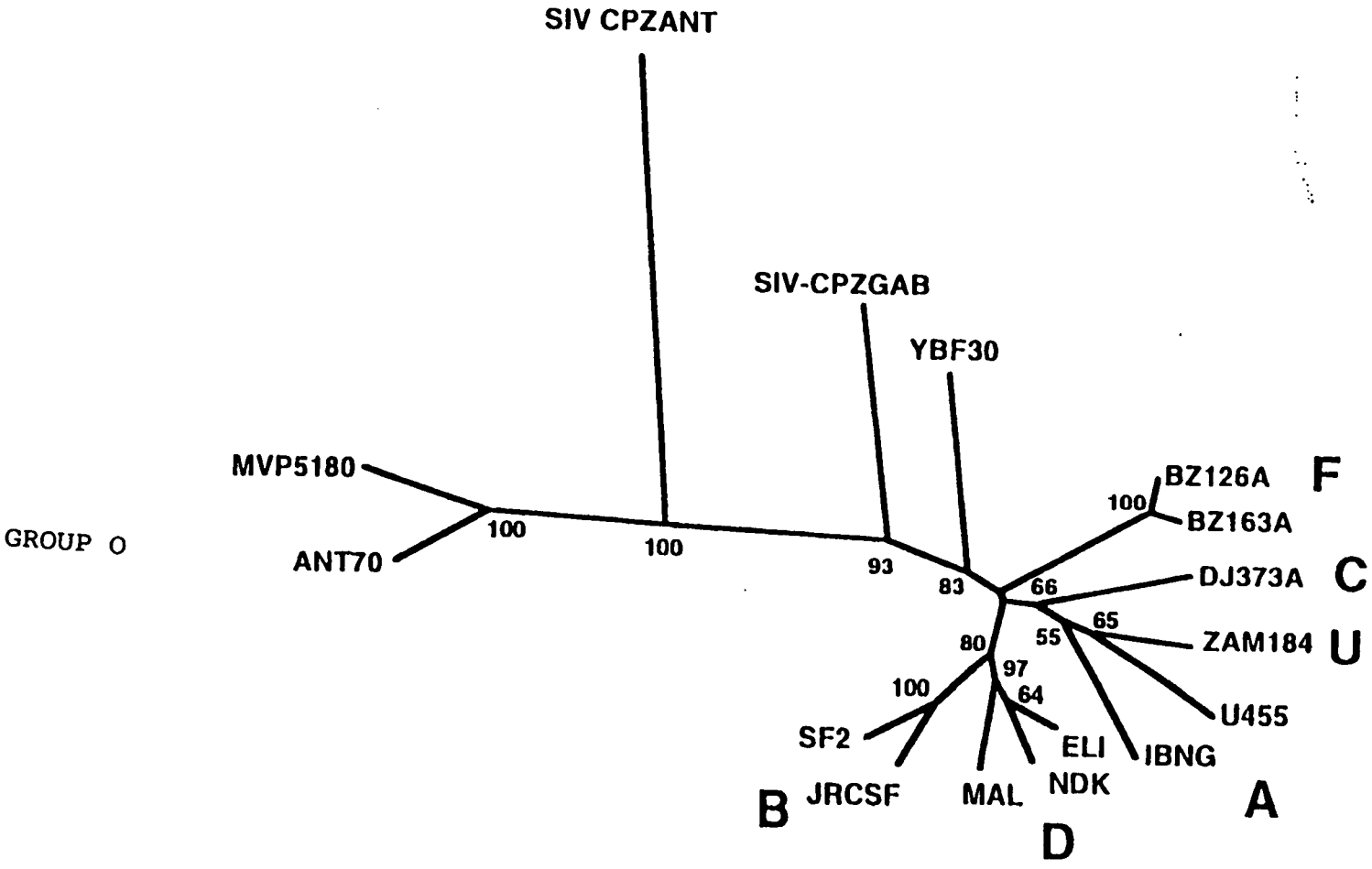


YBF30 Gag

1386 nt after "gapstripping" (after rearrangement of the alignment of the sequences)

Phylip n-j tree with "bootstrap" values (100 "bootstraps")

FIGURE 10



YBF30 Tat

292 nt after "gapstripping"

PHYLIP n-j tree with "bootstrap" values (100 "bootstraps")

FIGURE 11

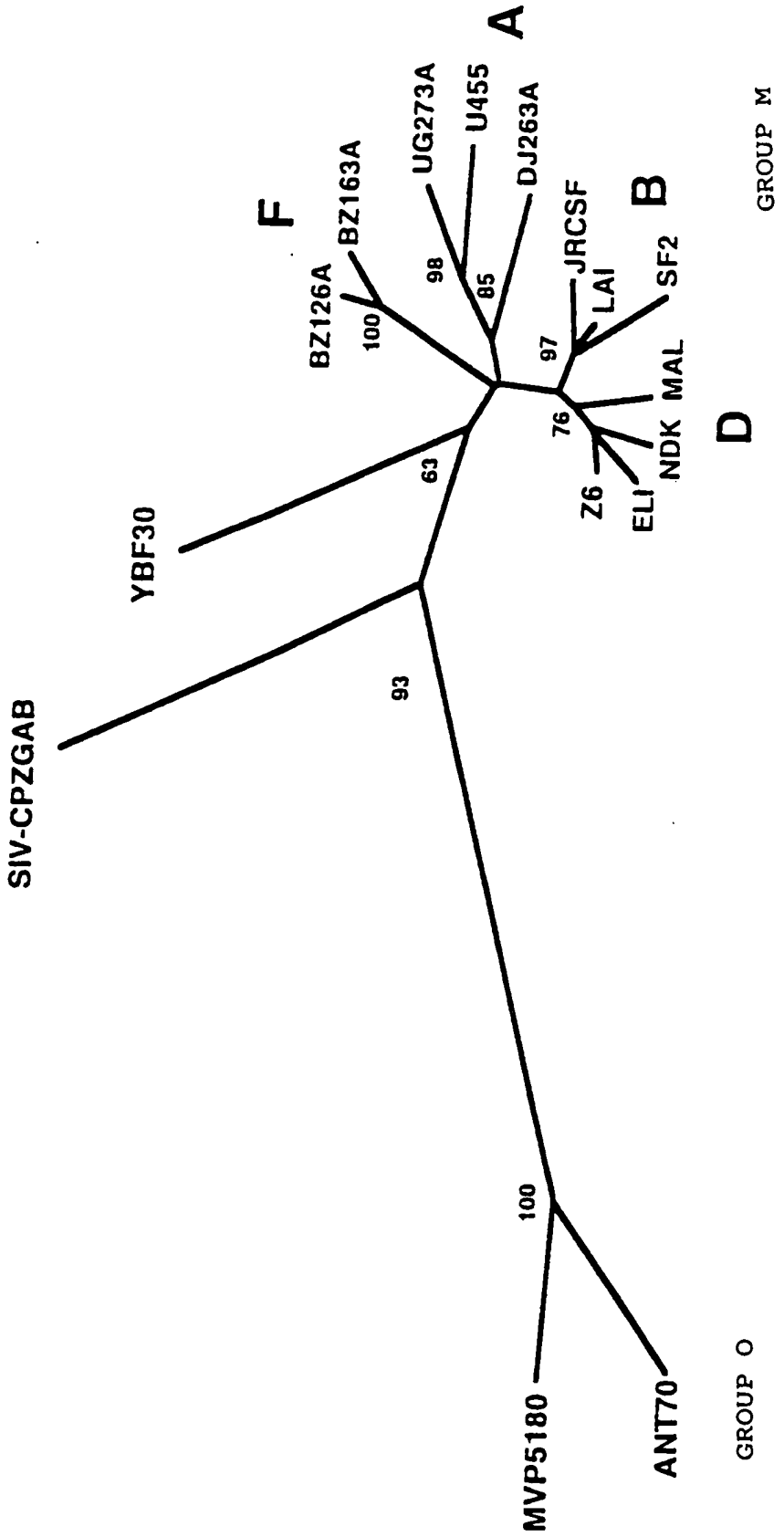


FIGURE 12

YBF30 Rev

296 nt after "gapstripping"

PHYLIP n-j tree with "bootstrap" values (100 "bootstraps")

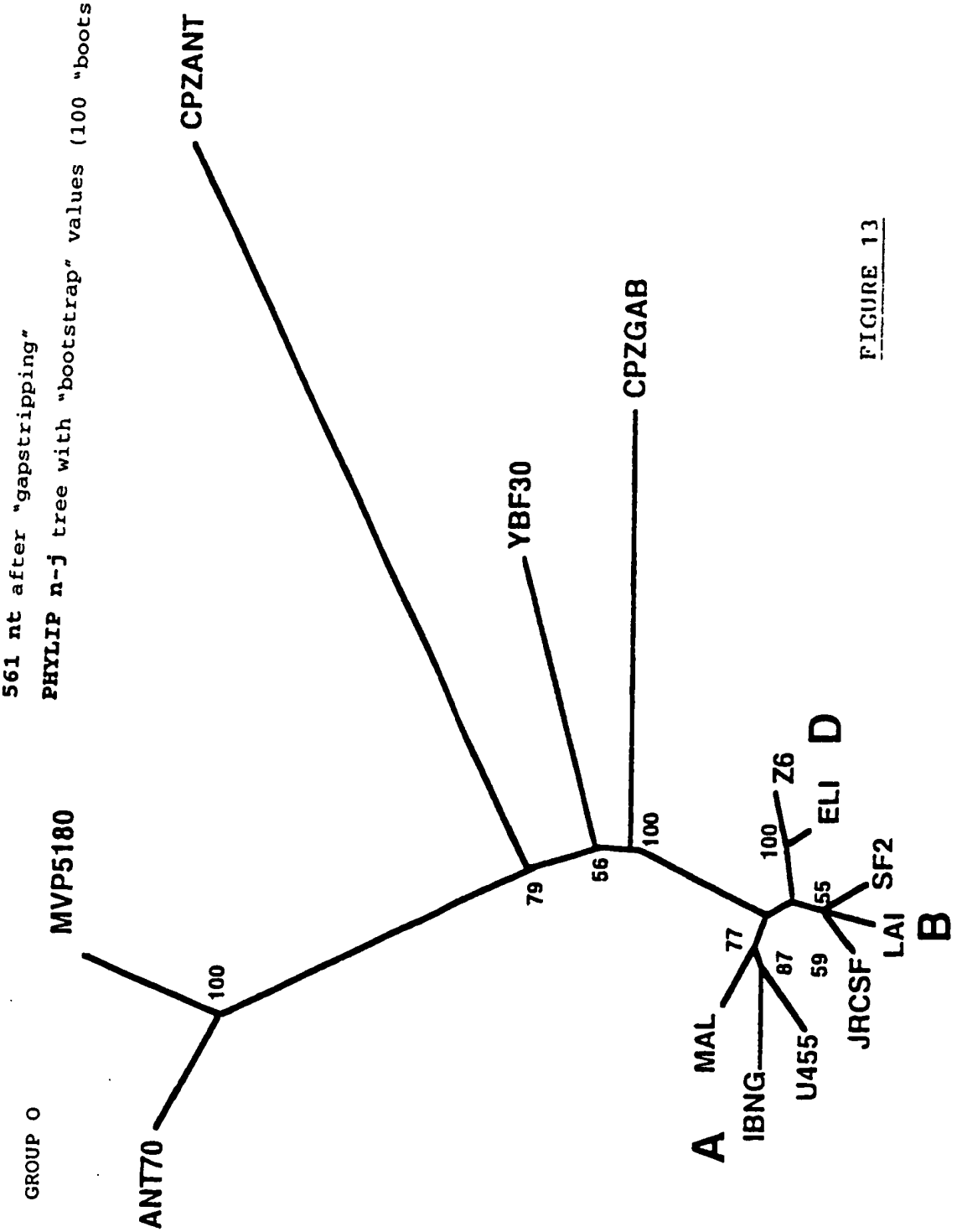
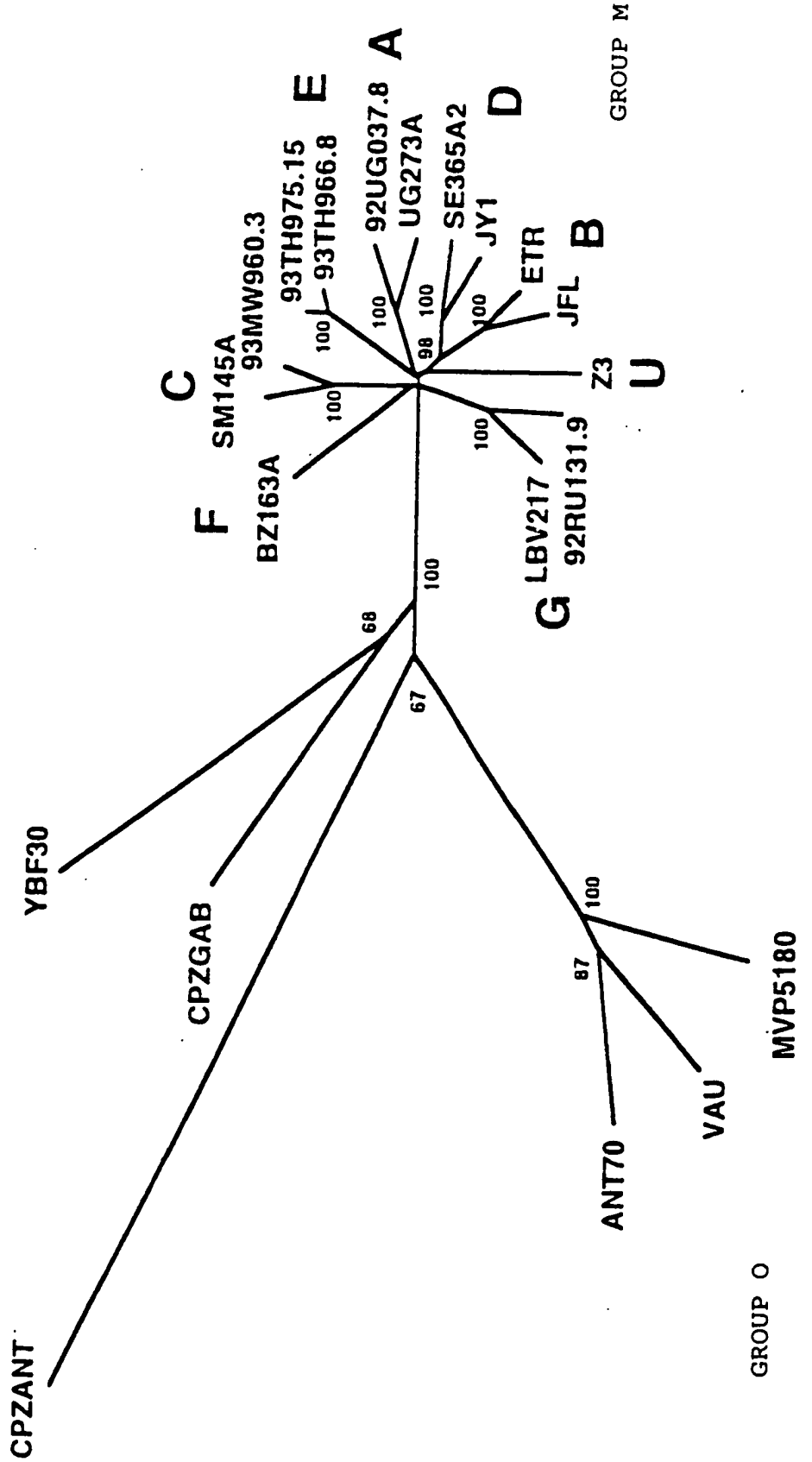

YBF30 Vif
561 nt after "gapstripping"
PHYLIP n-j tree with "bootstrap" values (100 "bootstraps")
GROUP O
ANT70
MVP5180
CPZANT
YBF30
CPZGAB
MAL
IBNG
U455
JRCSF
LAI
SF2
ELI
Z6
A
B
D
100
79
56
100
77
87
59
55
100

FIGURE 13



YBF30 gp120

1317 nt after "gapstripping"

PHYLIP n-j tree with "bootstrap" values (100 replicates)

Kimura distances, **transition/transversion = 1.8**

FIGURE 14

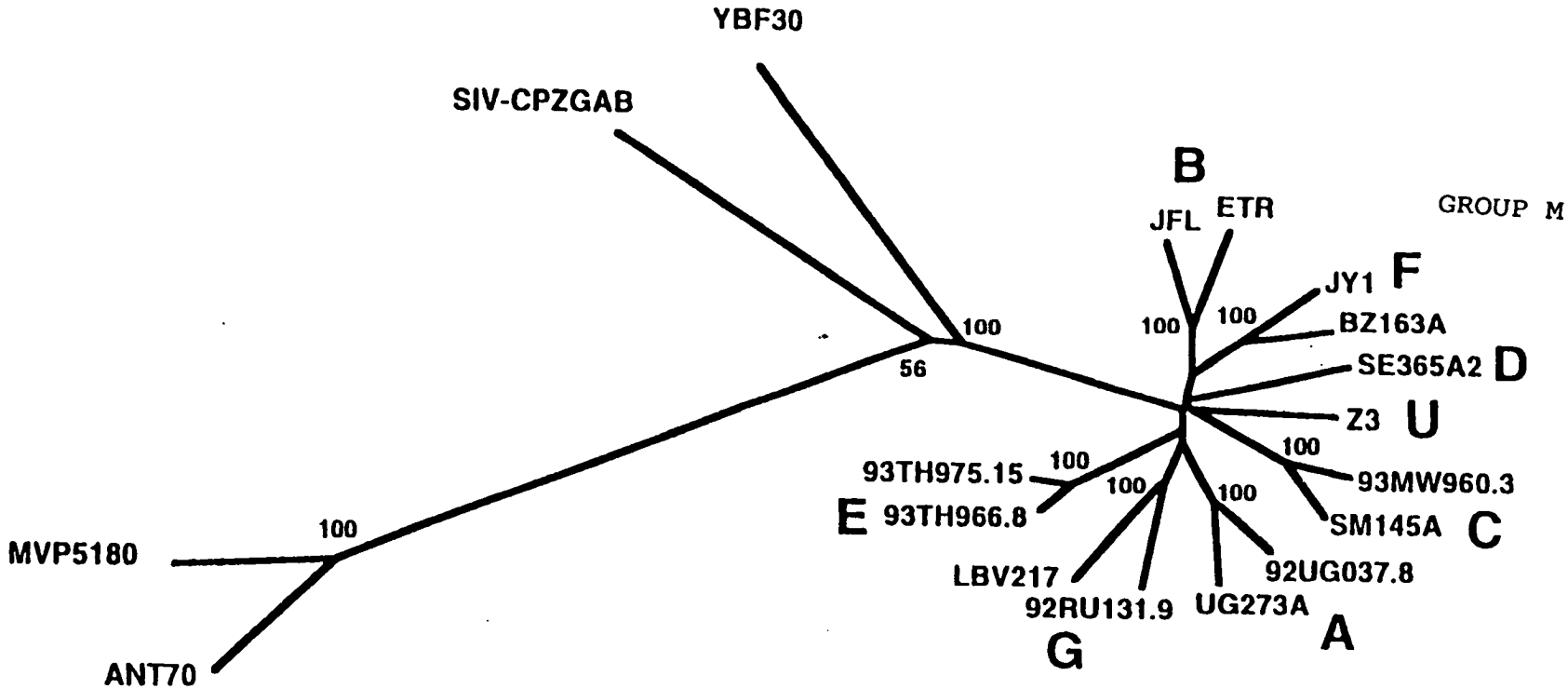
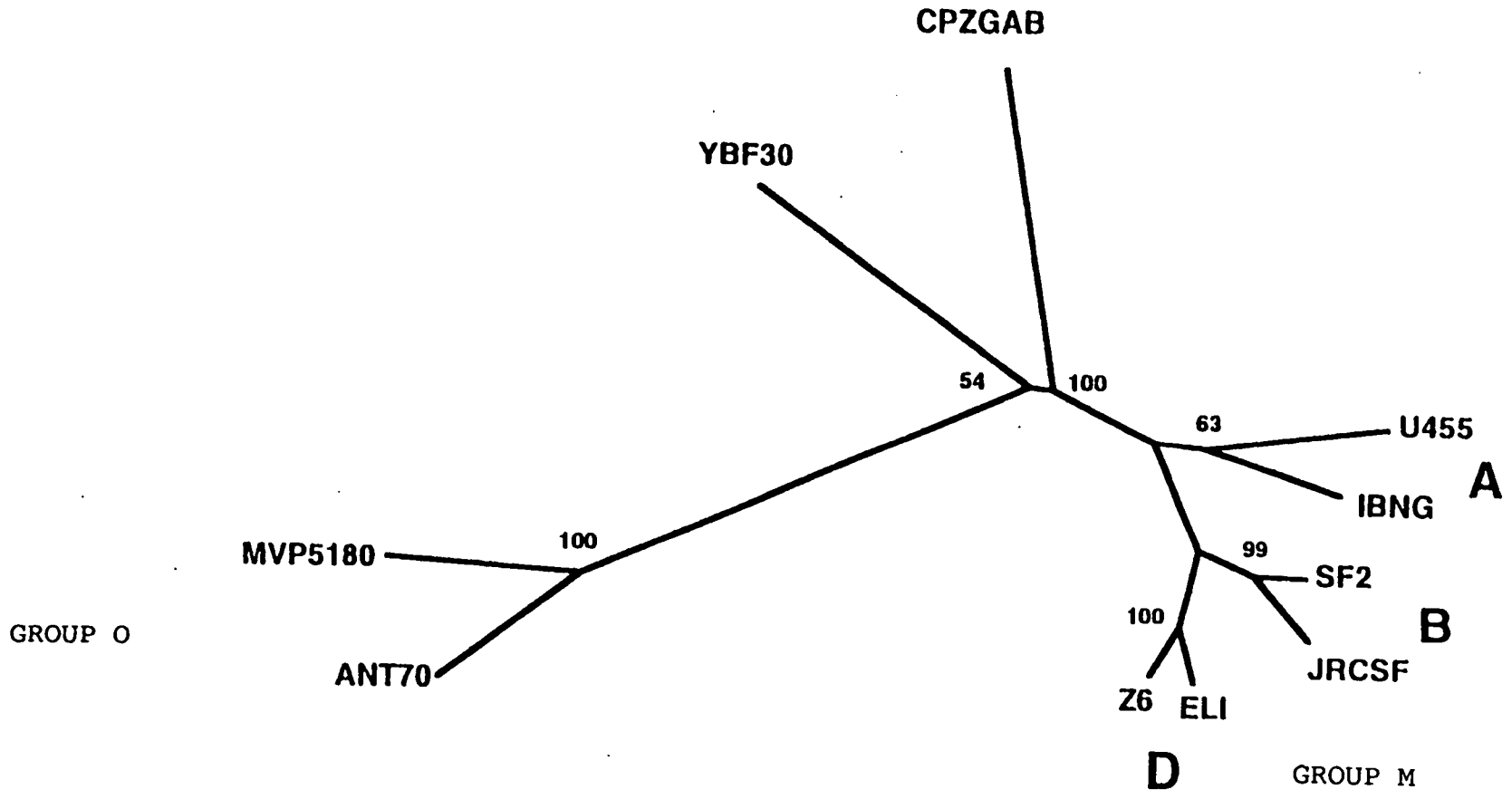


FIGURE 15

YBF30 gp41

988 nt after "gapstripping"

PHYLIP n-j tree with "bootstrap" values (100 "bootstraps")



YBF30 Nef

615 nt after "gapstripping"

PHYLIP n-j tree with "bootstrap" values (100 "bootstraps")

FIGURE 16

YBF30 POL

Phylip Fitch 1867 nt after "gapstripping"

(100 "bootstraps")

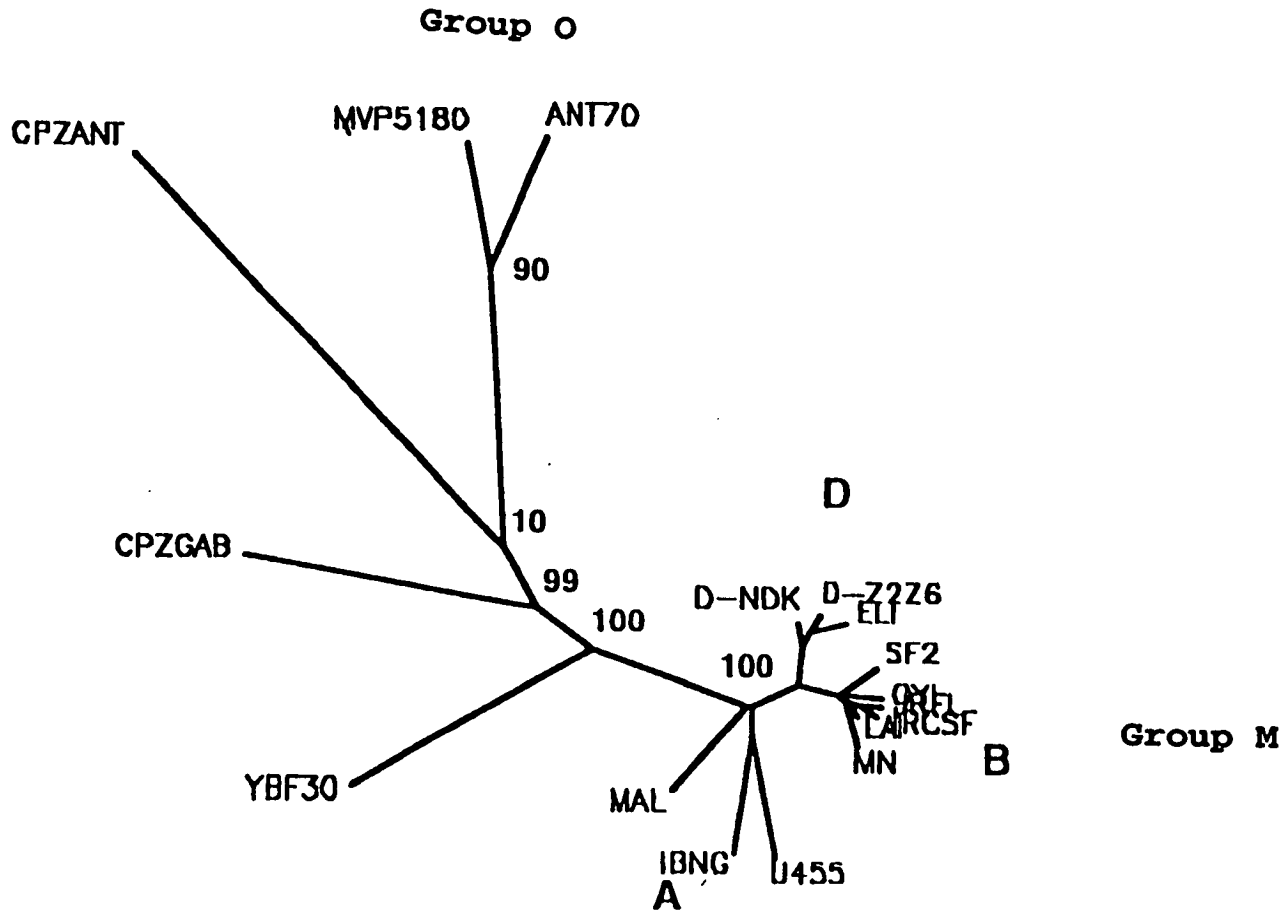


FIGURE 17

YBF30 VPR

Phylip nj, 315 nt after "gapstripping"

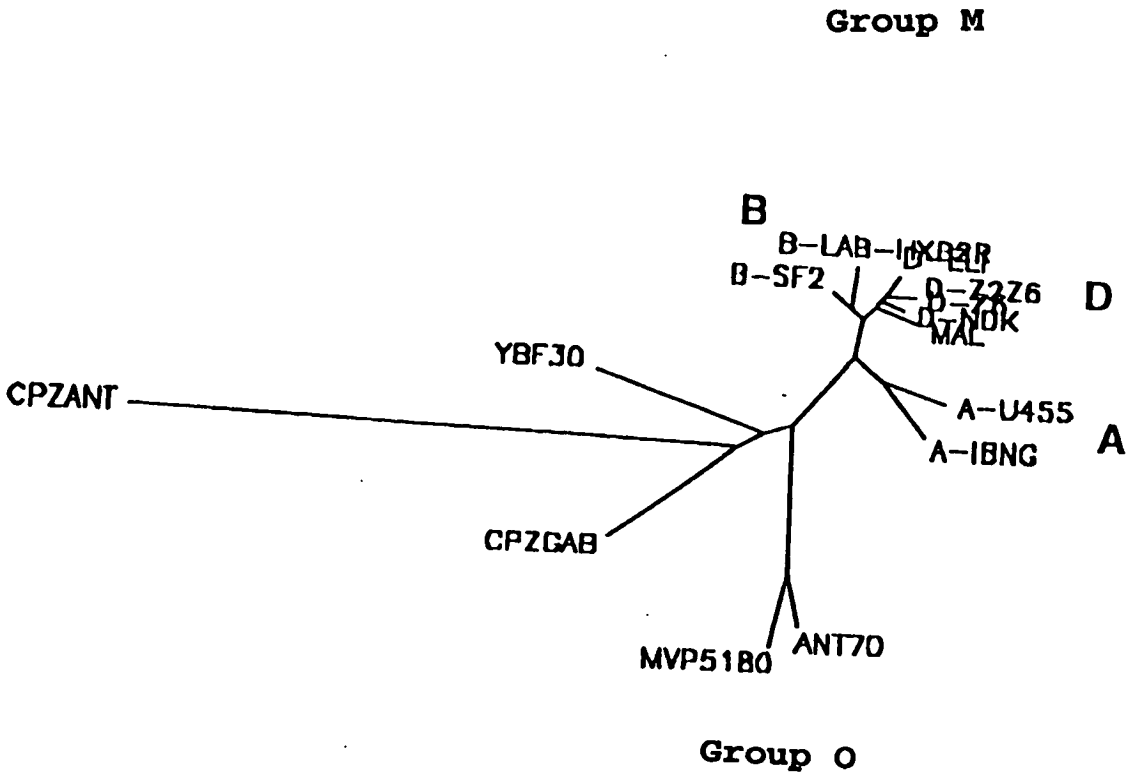
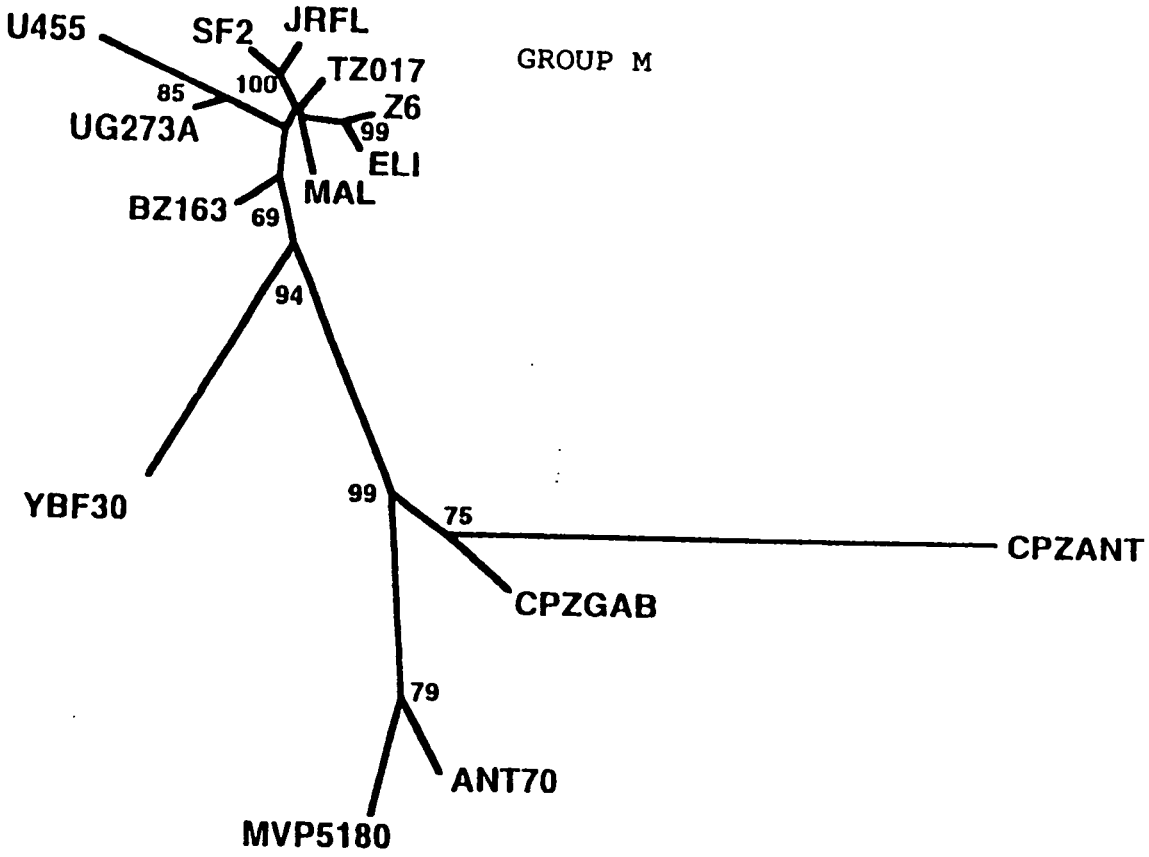


FIGURE 18



YBF30 Vpu

210 nt after "gapstripping"

PHYLIP n-j tree with "bootstrap" values (100 replicates)

FIGURE 19

Percentage genetic distance between YBF30 and HIV-1/CPZSIV

	Gag	Pol	Vif	Vpr	Vpu	Tat	Rev	Env gp120	Nef
HIV-1 M	30-33	22-24	27.5-30	27-30	66.6-80	22-27.6	33.8-42	50-53	34.6-39
HIV-1 O	37-38	33-34	42-45.6	32-36	>100	46-47.7	80-88	73-74	52.8-53
CPZGAB	32	26.8	40.3	28.8	>100	27.8	56.8	50	33.7
CPZANT	45	41.2	57.1	57.4	>100	55	ND*	74.5	ND*

* ND: not determined

FIGURE 20